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[54] **GENE FOR A GROWTH FACTOR AND ITS CDNA AND PROTEIN**

[75] Inventor: **Sandra J. Degen**, Cincinnati, Ohio

[73] Assignee: **Children's Hospital Medical Center**, Cincinnati, Ohio

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[58] **Field of Search** 530/399; 435/172.3, 435/69.4, 91, 320.1; 514/2.12; 424/69.4, 69.5; 536/23.5

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Primary Examiner—John Ulm

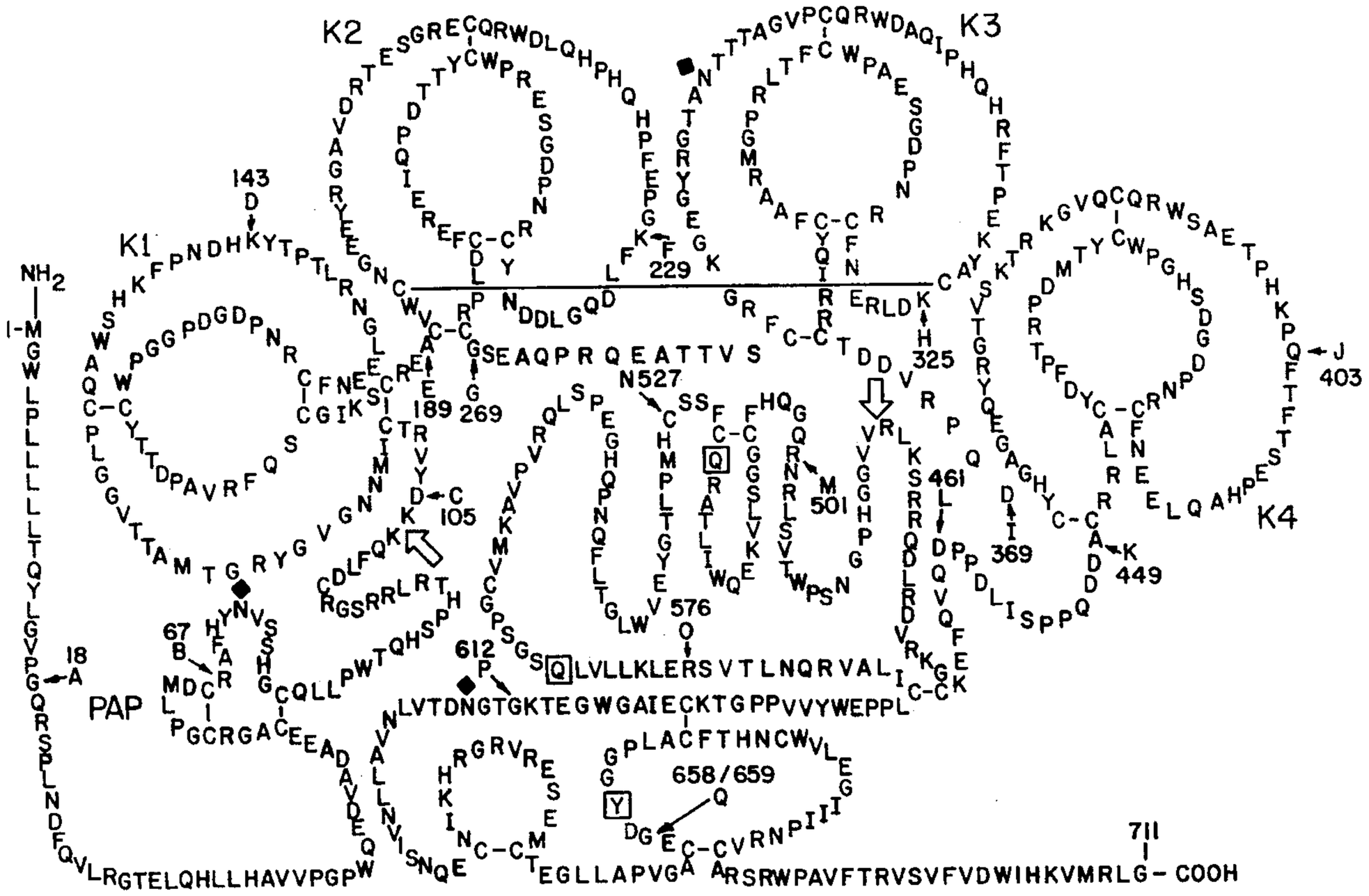
Assistant Examiner—Christine Saoud

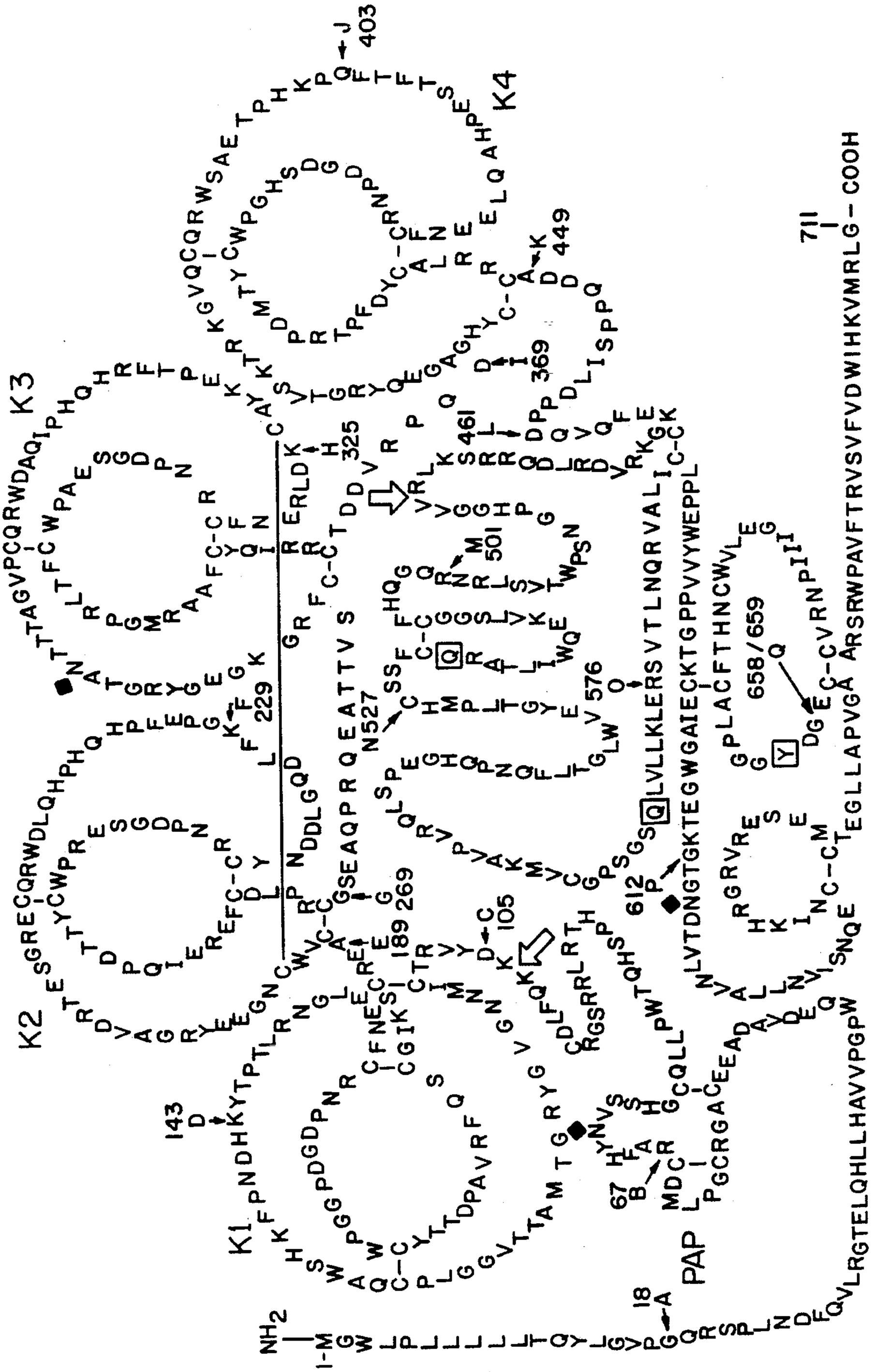
Attorney, Agent, or Firm—Wood, Herron & Evans, P.L.L.

[57] **ABSTRACT**

A growth factor protein similar in structure and function to hepatocyte growth factor has been discovered along with the DNA and cDNA coding for this in both the mouse and human. The DNA includes 18 exons and is homologous to DNA at the D3F15S2 locus on human chromosome 3; a region predicted to code for one or more tumor suppressor genes.

5 Claims, 1 Drawing Sheet





GENE FOR A GROWTH FACTOR AND ITS CDNA AND PROTEIN

This is a continuation of U.S. Ser. No. 07/882,925, filed May 14, 1992, now U.S. Pat. No. 5,315,000.

BACKGROUND

Growth factors are important for normal developmental processes, as well as for healing of wounds. Their abnormal expression has been implicated in neoplasia and other proliferative disorders. The kringle-containing protein hepatocyte growth factor (HGF) was originally identified as a potent growth factor involved in liver regeneration after liver injury or partial hepatectomy. It is now known that HGF functions as a growth factor for a broad spectrum of tissues and cell types. In addition, it has been recently discovered that HGF is identical to scatter factor (SF) a cytokine secreted from certain fibroblasts that enhances movement and causes the dissociation and scattering of epithelial cells (Gheradi & Stoker, 1990). The proto-oncogene c-met, a tyrosine kinase, has been found to be the cell surface receptor for HGF (Rubin et al., 1991; Bottaro et al., 1991). These properties may be important for metastasis of tumor cells.

In 1973 it was recognized that serum from partially hepatectomized rats stimulated hepatocyte proliferation in vitro (Morley et al., 1973). One of the agents responsible for this phenomenon was identified and isolated from such serum and from serum of patients with fulminant liver failure (Morley et al., 1973; Michalopoulous et al., 1984; Nakamura et al., 1984; Gohda et al., 1988). This agent was named hepatopoietin A or hepatocyte growth factor (HGF). HGF stimulates hepatocyte DNA synthesis and proliferation. Its serum concentration increases dramatically after rats undergo partial hepatectomy and decreases when the liver regenerates. HGF is produced by non-parenchymal liver cells (Schirmacher et al., 1992) and acts directly on hepatocytes in a paracrine fashion to stimulate cell multiplication. Although HGF stimulates growth of normal hepatocytes, it also has antiproliferative effects on hepatocarcinoma cells in culture (Tajima et al., 1991; Shiota et al., 1992).

HGF is a heterodimer of 82 kD composed of a α- and β-subunit with 51 kD and 26 kD molecular weight, respectively. The cDNAs for human and rat HGF have been cloned and characterized by several groups (Miyazawa et al., 1989; Nakamura et al., 1989; Okajima et al., 1990; Seki et al., 1990; Tashiro et al., 1990; Rubin et al., 1991).

HGF has no obvious homology with other known growth factors but is 38% homologous to plasminogen. It contains four kringle domains followed by a serine protease-like domain where the active site His and Ser have been changed to Gln and Tyr, respectively. HGF has no detectable protease activity. At present the function of the kringle domains in HGF is unknown.

Kringle domains were first identified in bovine prothrombin as an internal duplication of a triple-disulfide-bonded structure containing approximately 80 amino acids (Magnusson et al., 1975). Kringle domains were until recently only characterized in plasma proteins that functioned in blood coagulation or fibrinolysis (Davie et al., 1986) which includes prothrombin, Factor XII, urokinase-type plasminogen activator, tissue-type plasminogen activator and plasminogen. Recently, apolipoprotein(a) and HGF have also been shown to contain kringle domains. Apolipoprotein(a) is

thought to be involved in atherosclerosis (McLean et al., 1987). Kringle structures are thought to function autonomously (Trexler & Patthy, 1983; van Zonneveld et al., 1986) and fold independently (Tulinsky et al., 1988).

Kringles appear to be protein-binding domains and have been shown to be essential for the function of prothrombin, plasminogen and tissue plasminogen activator. The functions of all other kringle structures has not been determined, but since these structures are over 50% identical with each other, it is reasonable to assume that they are involved in binding interactions with other proteins essential for their regulation.

Two functional variants of HGF have been identified and have been found to be expressed at variable levels depending on the cell line or tissue being analyzed. A form of HGF containing the amino-terminal end of the protein including the first two kringle domains appears to result from alternative processing of the gene coding for HGF (Chan et al., 1991; Miyazawa et al., 1991). This variant binds to the c-met receptor although not as effectively as the full-length protein. Another variant has a five amino acid deletion in the first kringle domain that appears to have no effect on its activity (Seki et al., 1990; Rubin et al., 1991). Specific domains in HGF have been deleted by using techniques in molecular biology and the resultant proteins have been studied in various assays where native HGF can be measured. Matsumoto et al. (1991) concluded that the amino-terminal portion of the protein including the first and second kringle domains are essential for biological activity of HGF and possibly binding to the receptor.

Chromosomal abnormalities in a number of neoplastic diseases are sometimes associated with the activation of a proto-oncogene or the loss of a gene that suppresses tumor growth. Growth factors are important for normal developmental processes, as well as healing of wounds. Their abnormal expression has been implicated in neoplasia and other proliferative disorders (Aaronson, 1991). Growth factors are involved in signaling pathways that influence normal cellular differentiation. These proteins cause cells in the resting phase (Go) to enter and progress through the cell cycle. oncogenic mutations in several growth factors result in unregulated cell growth. Tumor suppressor genes are genes expressed in normal cells that play regulatory roles in cell proliferation, differentiation and other cellular events. Loss or inactivation of these genes is oncogenic. Tumor suppressor genes that have been extensively characterized include the genes for colon carcinoma, retinoblastoma, type 2 neurofibromatosis, the genes involved in Wilms tumor and the p53 gene (reviewed in Weinberg, 1991). Tumor suppressor genes are involved in cell cycle control, signal transduction, angiogenesis, and development (Sager, 1989; Weinberg, 1991).

The concept that the loss of genetic material or the inactivation of a gene plays an important role in human cancer is based on the original observation that somatic cell hybrids between tumor cells and normal cells were no longer tumorigenic. This indicated that normal cells contain genes coding for tumor suppressors whose function was absent in cancer cells. In addition, cytogenic and restriction fragment length polymorphism (RFLP) analyses have established an association between the loss of genetic material on specific chromosomes and the development of various human malignancies.

Deletion of the short arm of human chromosome 3 has been implicated in small cell lung carcinoma (SCLC; Whang-Peng et al., 1982; Naylor et al., 1987), other lung

cancers (Kok et al., 1987; Brauch et al., 1987), renal cell carcinoma (Zbar et al., 1987; Kovacs et al., 1988) and yon Hippel-Lindau syndrome (Seizinger et al., 1988) which suggests that one or more tumor suppressor genes reside on chromosome 3p which manifest their transformed phenotype upon their inactivation. The chromosomal locus DNF15S2 (also called D3F15S2) is a RFLP probe that most consistently is associated with loss of heterozygosity in SCLC, being detected in virtually 100% of SCLC.

Lung cancer is a common human malignancy with 150,000 new cases reported each year in the United States. Unfortunately, 90% of affected persons will die within 5 years of diagnosis. Mortality due to lung cancer has increased more than 15% since 1973. Increases in cigarette smoking from 1900 until the early 1960s has transformed lung cancer from a rare disease at the turn of the century to the current leading cause of cancer death. In women, lung cancer surpassed breast cancer as the leading cause of cancer death in 1986 with rates expected to continue to increase for at least another ten years (Henderson et al., 1991).

Lung cancer is divided into small cell and non-small cell varieties. The non-small cell lung cancers include adenocarcinoma, squamous and epidermoid lung cancer and large-cell lung cancer. Chromosome 3p(14–23) changes have been found in nearly all small cell lung cancers and in a large fraction of non-small cell lung cancers.

Cancer of the kidney accounts for 1–2% of all malignancies (excluding skin cancer) with renal cell carcinoma comprising 85% of these. Renal cell carcinoma (RCC) occurs in sporadic and familial forms and are commonly seen in the age group between 50 to 70 years. Cigarette smoking is a known risk factor for this form of cancer (Walter et al., 1989). Deletion of the short arm of chromosome 3 is the most commonly involved region of the genome in RCC and therefore appears to play a role in the development and/or progression of this form of cancer.

Several genes have been localized near or at the D3F15S2 locus. The ERβEAB locus coding for a DNA-binding thyroid hormone receptor is localized to human chromosome 3p21–25, and overlaps deletions found in SCLC. Leduc et al. (1989) determined that many non-SCLC tumors retained both ERBAB alleles while the D3F15S2 locus was reduced to homozygosity, ruling out a role for the thyroid hormone receptor in this form of cancer. The gene encoding aminoacylase-1 at 3p21 is inactivated in a large fraction of SCLC (Naylor et al., 1982, 1989). A similar allelic loss is observed in sporadic renal cancers and there are cytogenetic abnormalities of this region in familial renal cell cancer. The gene coding for protein-tyrosine phosphataseγ (PTPγ) maps to 3p21 (LaForgia et al., 1991). This protein and homologous family members reverse the effect of protein tyrosine kinases, of which, some have been identified as oncogenes (ie., met, fms, kit, ERBB). In one study, one PTPγ allele was deleted in 3 of 5 renal carcinoma cell lines and in 5 of 10 lung carcinoma samples tested (LaForgia et al., 1991). In summary, the key gene(s) responsible for tumor suppressor activity at this locus is unknown, although there are some candidate genes.

SUMMARY OF THE INVENTION

The present invention is based on the isolation and characterization of the human gene located at the D3F1552 locus on human chromosome 3 referred to as L5/3. The protein coded for by this gene is referred to as the L5/3 protein. The translated amino acid sequence indicates that L5/3 protein is composed of four kringle structures followed by a serine protease-like domain. This is identical in composition to hepatocyte growth factor (HGF) although L5/3 protein and HGF are only 50% identical to each other when their amino acid sequences are compared. The corresponding human cDNA has also been isolated, as well as the mouse gene and cDNA.

The L5/3 protein can be employed to alter cell growth (as a growth factor or tumor suppressor). The L5/3 protein has properties similar to HGF that is actively involved in liver regeneration.

In addition, the L5/3 gene is identical to the gene at a locus on human chromosome 3 (3p21) that is deleted in DNA from all small cell lung carcinomas and has been hypothesized to contain one or more tumor suppressor genes. Thus this isolated gene L5/3 can be used as a probe to provide an indication of a predisposition for certain cancers. Further, identification of the coded L5/3 protein can also be utilized to evaluate a predisposition to cancer.

BRIEF DESCRIPTION OF THE DRAWINGS

The FIGURE is a schematic diagram of the amino acid sequence of human L5/3, SEQ ID NO:8.

DETAILED DESCRIPTION OF THE INVENTION

The methods discussed below to obtain DNA sequences encoding L5/3 are merely for purposes of illustration and are typical of those that might be used. However, other procedures may also be employed.

The human L5/3 gene was isolated using a multistep process employing various DNA and cDNA probes which were both of human and mouse origin. Further, the initial probe is a bovine prothrombin cDNA.

A human liver genomic DNA library cloned into bacteriophage Charon 28 (Lawn et al., 1978) was obtained from Dr. Tom Maniatis, Harvard University (this library is presently available from the ATCC). This library is an Alu/Hae III fetal human genomic DNA library. The library containing approximately 2×10^6 recombinant phage was plated out on *E. coli* strain LE392 and grown overnight at 37° C. and was screened by the in situ plaque hybridization technique of Benton & Davis (1977) as modified by Woo (1979).

Approximately 1×10^8 cpm of nick-translated bovine prothrombin cDNA probe (obtained by Ava I and Bam HI digestion of pBII102; this probe is 1200 bp in length coding for amino acids 109–500; MacGillivray & Davie, 1984) was hybridized to nitrocellulose filters containing the recombinant phage under conditions of reduced stringency. These conditions included hybridization at 60° overnight in 2×Denhardt's solution (0.04% polyvinylpyrrolidone, 0.04% Ficoll and 0.04% bovine serum albumin) containing 6×SSC [1×SSC: 0.15M sodium chloride and 0.015M trisodium citrate (pH 7.0)], 1 mM EDTA and 0.5% sodium dodecyl sulfate (SDS). The filters were washed three times at 60° C. in 6×SSC with 0.5% SDS. Twelve positive phage were identified. Two of these phage have been identified to code for the human L5 gene.

This human L5 gene and its method of selection is also disclosed in the doctoral thesis of Sandra J. Friezner Degen entitled *Isolation* and *Characterization of the Human Prothrombin Gene* And *Related Genes* published in 1982. As discussed below this gene characterized as L5 is an incomplete gene but is useful in isolation and characterization of

the gene of the present invention. Until now its function was also unknown.

The obtained L5 gene was then used to obtain the corresponding human L5 cDNA. The human cDNA corresponding to the L5 gene was used to obtain the mouse cDNA. This mouse cDNA was in turn used to obtain the mouse L5/3 gene. The mouse L5/3 gene was used to obtain the human L5/3 gene.

A λgt11 cDNA library prepared from human fetal liver mRNA (provided by Dr. Vincent Kidd, University of Alabama, Birmingham; Kwok et al., 1985) was screened for the human cDNA coding for L5 by using a probe isolated from the human L5 gene (680 bp Bam HI and Hind III fragment isolated from a 1850 bp subclone (obtained by digestion of L5 with Hind III and cloning into pBR322) and coding for part of the second kringle and all of the third; nucleotides 2190–2868 of Sequence ID No. 6). Approximately 1×10^5 phage were screened at high stringency using standard techniques (Degen & Davie, 1987). These conditions include hybridization with the same solution used for isolation of the human L5 gene discussed above but at 68° C. and washing at 68° C. in 1×SSC containing 0.5% SDS. Six positives were identified. The longest (#46) was 1.9 kb in length. A 5'-end fragment from this cDNA (340 bp Eco RI and Nco I fragment coding for part of kringles 1 and 2; nucleotides 388–733 in sequence ID No. 1) was used to rescreen the library to obtain clones with longer 5' ends. Two clones (#33 and #19) were identified and characterized (Sequence ID No. 1,2,3). The longest clone (#33) is 2200 bp in length excluding the poly(A) tail and is not full-length since its 5' end starts 16 bp downstream from the putative initiator methionine codon in the first exon of the gene (starting at nucleotide 290 in Sequence ID No. 6).

A γgt10 mouse liver cDNA library (Stratagene, La Jolla, Calif.; from mouse strain C57BL/6) was then screened using a fragment from the human cDNA #33. Approximately 1×10^6 phage were screened with a probe isolated from the 5' end of the human cDNA (the 340 bp fragment was isolated from human cDNA-33 after digestion with Eco RI and Kpn I and coded for the amino-terminal portion of the protein including eight amino acids of the first kringle; nucleotides 1 to 334 in Sequence ID No. 1) using the conditions of reduced stringency discussed above for the isolation of the human L5 gene. These conditions were used to allow for cross species hybridization. Ten positives were identified and eight were characterized after cloning the cDNAs into pBR322.

The longest cDNA (pML5-2) was 2188 bp in length and was not full-length since the open reading frame was present at the 5' end of the sequence with no codon for the initiator methionine in-frame with the coding sequence (Sequence ID No. 4). After determination of the sequence of the mouse gene it was determined that the cDNA lacked 44 bp of coding and 94 bp of 5' noncoding sequence at its 5' end.

A mouse liver genomic DNA library cloned into the Bam HI site of EMBL-3 SP6/T7 (Clontech; mouse strain Balb/c; catalog #M 1030 J) was screened for the gene coding for mouse L5/3. Approximately 1×10^6 phage from the library were screened with a probe isolated from the previously isolated mouse cDNA (the 1450 bp insert was isolated from pML5-2 after digestion with Eco RI and coded for eight amino acids of the second kringle, all of the third and fourth kringles and the serine protease-like domain; nucleotides 738 to 2188 in sequence ID No. 4) using the identical high stringency conditions discussed above for the isolation of the human L5 cDNA. On the initial screen, 65 positives were identified; 9 were characterized. Restriction fragments of phage DNA were subcloned into pBR322.

A second human genomic DNA library prepared from placental DNA using EMBL-3 SP6/T7 as the cloning vector (Clontech; catalog #HL 1067 J) was screened for the 5' end of the gene coding for L5/3 with a mouse genomic fragment containing the first exon of the gene for mouse L5/3. This fragment was 400 bp in length and was isolated by digestion of a genomic subclone from the mouse gene (a 3.3 kb Bgl II fragment cloned into the Bam HI site of pBR322) with Bam HI and Eco RI (nucleotides 1086–1486 in Sequence ID No. 5). Approximately, 500,000 recombinant phage were screened under identical reduced stringency conditions discussed above for the original isolation of the L5 gene. Thirteen positives were identified; three were characterized and found to code for the 5' end of the human L5/3 gene (referred to as L3).

Fragments from two overlapping phage (L5 and L3) were subcloned into pBR322 and the DNA sequence of the inserts were determined. The entire sequence of the gene present in L5 and L3 is shown in Sequence ID No. 6. This gene is the complete gene L5/3 of the present invention. The gene is 4690 bp in length (from the codon for the putative initiator methionine to the polyadenylation site; nucleotides 274–4963 in Sequence ID No. 6). The gene is composed of 18 exons separated by 17 intervening sequences. In addition, sequence has been determined both upstream and downstream of the gene.

The 3' end of the acyl-peptide hydrolase gene is 444 base pairs downstream of L5/3 gene on the complementary strand (nucleotides 5408 to 6100 in Sequence ID No. 6).

Several isolated cDNA fragments were characterized. One cDNA (#19) had two parts of the coding region deleted when compared to cDNA (#33) which included nucleotides 1366–1486 and 1565–1613 in Sequence ID No. 1. The cDNA for #19 is Sequence ID No. 3. In the L5/3 gene the region deleted included exon 13 (nucleotides 3532–3652 in Sequence ID No. 6) and the 5' end of exon 18 (nucleotides 4033–4081 in Sequence ID No. 6). If this cDNA represents a translated mRNA, it would code for the four kringle domains followed by only 22 amino acids since there are two in-frame stop codons at that point.

Comparison of all cDNA sequences indicates that at least five polymorphisms occur; only one of which results in an amino acid substitution. This substitution is a Cys (Sequence ID No. 1) to Phe (Sequence ID No. 2) at amino acid residue 212. When the sequence of the exons in the L5/3 gene are compared to the cDNA sequences, one additional polymorphic site is identified that results in a Tyr (in the cDNAs; Sequence ID No.1 and Sequence ID No. 2) to Cys (in the gene; Sequence ID No. 6) substitution at residue 13. All of these polymorphisms should occur in the population and all would represent functional L5/3 protein.

The gene and cDNA coding for L5/3 codes for a protein with similar domain structure as HGF with four kringles followed by a serine protease-like domain. The translated amino acid sequences of the gene (shown in the FIGURE) and cDNA for human L5/3 predict a protein with 80,325 molecular weight containing 711 amino acids (excluding additional post-translational processing). The FIGURE is a schematic diagram of the amino acid sequence of human L5/3. The amino acid sequence of human L5/3 is shown starting with residue 1 at the amino-terminal end and ending with residue 711 at the carboxy-terminal end. Placement of disulfide bonds was determined solely on the basis of homology with this protein sequence to plasminogen, where

placement of disulfides has been determined. The four kringle domains are indicated by K1, K2, K3, and K4. The region homologous to the preactivation peptide of plasminogen is indicated by PAP. The three potential N-linked cleavage sites are indicated by open arrows. The sequence following the second open arrow is homologous to other serine proteases. The active site amino acids His, Asp and Ser have been changed to Gln, Gln and Tyr, respectively and are indicated in boxes. Amino acids are represented in the one letter code where A-Ala, C=Cys, D=Asp, E=Glu, F=Phe, G=Gly, H=His, I=Ile, K=Lys, L=Leu, M=Met, N=Asn, P=Pro, Q=Gln, R=Arg, S=Ser, T=Thr, V=Val, W=Trp and Y=Tyr. There are three potential carbohydrate additions sites at asparagines in the sequence Asn-X-Thr/Ser at positions 72, 296 and 615 (in the FIGURE). The sequence at the amino-terminal end of the putative protein is hydrophobic and therefore may be part of a signal sequence required for secretion of the protein from the cell. Comparison of the amino-terminal sequence to a consensus sequence compiled for known signal peptidase cleavage sites (Von Heijne, 1983; Watson, 1984) predicts that the cleavage site could be between residues Gly-31 and Thr-32 (in the FIGURE). The active protein coded by the L5/3 gene refers to the protein as modified during expression and passage through the cell wall. Thus the active protein would exclude the signal sequence which may include residues 1–31.

Based on homology to plasminogen and other serine proteases, two additional proteolytic cleavage sites are predicted. Between the kringle domain region and the serine protease-like domain is an amino acid sequence that is typically found at the activation sites of other coagulation and fibrinolytic proteins with serine protease activity. Residue 483 is an Arg followed by the sequence Val-Val-Gly-Gly that is typically found at the amino-terminal end of serine proteases (in the FIGURE). On the basis of this sequence, it is anticipated that active L5/3 protein is proteolytically cleaved to yield a two-chain molecule held together by disulfide bonds or cleaved into two separate polypeptide chains. Amino acid residues 56–103 in human L5/3 are homologous to the preactivation peptide (PAP) in plasminogen and HGF (in the FIGURE). The PAP region in plasminogen is between the amino-terminal end of the mature protein and the plasmin activation site between Lys-77 and Lys-78. Both lysines are conserved in L5/3 (residues 103 and 104 in the FIGURE). Cleavage at this site would remove a peptide of 103 amino acids from the protein (including the putative signal peptide) if it is not disulfide-bonded to the remainder of the protein (there is one additional cysteine in this region).

The amino acids found in the active site of serine proteases have been changed from His to Gln, Asp to Gln, and Ser to Tyr at positions 522, 568, and 661, respectively (in the FIGURE). Therefore, we anticipate that this protein has no proteolytic activity.

Only a portion of the entire primary structure may be required for function. Also included within the definition the active proteins coded for by the L5/3 gene are fragments of the entire sequence which retain activity particularly those which result from post-translational processing such as glycosylation. It is further understood that minor modifications of primary amino acid sequence may result in proteins which have substantially equivalent or enhanced activity as compared to any particular illustrated sequence. These modifications may be deliberate, as through site-directed mutagenesis, or may be accidental, such as mutations of hosts which are L5/3 producing organisms. All of these modifications are included as long as the activity of the L5/3 protein is retained.

The complete mouse L5/3 DNA sequence and the amino acid coding regions of the gene are shown in Sequence I.D. No. 5. The mouse L5/3 gene is composed of 18 exons separated by 17 intervening sequences. The gene is 4613 bp in length from the site of initiation of transcription to the polyadenylation site. (Nucleotides 1192 to 5804 in Sequence ID No. 5.) The gene coding for acyl-peptide hydrolase is 410 base pairs downstream of the L5/3 gene, but is transcribed from the complementary strand (nucleotides 6215–6751 in Sequence ID No. 5).

The mouse cDNA (Sequence ID No. 4) codes for a putative protein with the same domain structure as its human homolog with four kringle domains followed by a serine protease-like domain. Translated sequence from the gene and cDNA coding for mouse L5/3 indicate that a protein of 716 amino acids with a molecular weight of 80,593 would be synthesized (excluding any additional post-translational processing). There are four potential N-linked carbohydrate attachment sites at asparagines in the sequence Asn-X-Thr/Ser at positions 72, 173, 305 and 624. The sequence at the amino-terminal end of the putative protein is hydrophobic and therefore may be part of a signal sequence required for secretion of the protein from the cell. Based on homology with the human cDNA the signal peptidase cleavage site is between amino acid residues Gly-31 and Thr-32 Sequence ID No. 4.

There is only one difference found when the sequences of the cDNA and gene coding for mouse L5/3 are compared which results in the substitution of a Gln in the gene (Sequence ID No. 5) to a Pro in the cDNA (Sequence ID No. 4) at residue 19. It is anticipated that this site is polymorphic in the population and that both are representatives of functional L5/3 protein.

The primary site of synthesis of mRNA for L5/3 is in the liver as determined by analysis of rat tissue RNA by Northern analysis. Lesser amounts of L5/3 mRNA were found in the lung, adrenal, and placenta.

A fusion protein was produced as well as polyclonal antibodies. A 968 bp fragment from the human L5/3 cDNA (#33) was obtained after digestion with Bam HI and Bgl II and cloned into the prokaryotic expression vector pUR278 (Ruther & Muller-Hill, 1983). This fragment represents nucleotides 746–1714 in Sequence ID No. 1 and codes for part of kringle 2, all of kringles 3 and 4 and part of the serine protease-like domain of L5/3. In pUR278, the L5/3 cDNA fragment was cloned into the Bam HI site near the 3' end of the lac Z gene to allow for expression of an active β-galactosidase fused with the peptide encoded by the L5/3 cDNA fragment in *E. coli.* The correct reading frame was maintained in the construct as determined by DNA sequence analysis. The 968 bp insert codes for 321 amino acids (residues 255–576 in Sequence ID No. 1) with a calculated molecular weight of approximately 35,000 daltons. The predicted size for the fusion protein is approximately 151,000 daltons which contains the human L5/3 protein peptide fused to β-galactosidase (116,000 MW).

The fusion protein was isolated and electroeluted after SDS-polyacrylamide gel electrophoresis of isopropyl thiogalactoside (IPTG) induced *E.coli* cell extract from cells that had been transformed with the fusion construct.

Fusion protein (β-galactosidase/L5/3) was injected into New Zealand rabbits in order to obtain polyclonal antibodies against the fusion protein by standard techniques.

Tissue lysate from human liver and human plasma were electrophoresed on SDS-polyacrylamide gels under reducing condition, transferred to an Immobilon-P membrane

(Amersham, Inc.) and reacted with rabbit anti-β-galactosidase/human L5/3 fusion protein serum. The antibody reacted primarily with a polypeptide of approximately 84,000 molecular weight in plasma and to a lesser extent with a polypeptide of 60,000 molecular weight. Non-immune serum did not react with polypeptides of these sizes on either reducing or non-reducing gels. The antibody did not react with any detectable protein in the liver extract. The antibody did not cross react with purified human prothrombin. On non-reducing gels the antibody detected a protein of approximately 90,000 molecular weight.

These results are consistent with the presence of a signal peptide at the amino-terminal of L5/3 that is required for secretion from the cell since the antibody reacted only with a polypeptide present in plasma and not in liver extract. The signal peptide of approximately 3500 daltons would be removed before secretion from the cell. In addition, these results are consistent with proteolysis at possibly both of the putative proteolytic sites present in L5/3 (in the FIGURE). Based on the translated cDNA sequence, the full-length protein would be approximately 80,000 daltons. Carbohydrate addition to some or all of the three possible N-linked glycosylation sites might increase the molecular weight to the approximately 90,000 dalton size seen in plasma on non-reducing gels. On reducing gels where the disulfide bonds have been removed, the 84,000 molecular weight protein could be the result of proteolytic cleavage between amino acid residues 103 and 104 (Sequence ID No. 1 in the FIGURE). The predicted size of the protein with the amino-terminal 103 residues removed is approximately 70,000 daltons. The 84,000 molecular weight protein may be this fragment of L5/3 after glycosylation. On non-reducing gels this fragment could possibly be disulfide-bonded to the remainder of the protein (there is one additional cysteine in this part of the protein that could be involved in disulfide formation) and may be the reason why a larger protein was observed on the non-reduced gel compared tO the reduced one. The 60,000 dalton polypeptide also seen in plasma on reducing gels could be the result of additional proteolytic cleavage of the protein between residues 483 and 484 (Sequence ID No. 1 in the FIGURE) which is a typical serine protease activation site. The resultant fragments would have molecular weights of 50,000 and 25,000 daltons (excluding any post-translational modifications such as glycosylation). If the two potential N-linked carbohydrate addition sites in the 50,000 dalton fragment are glycosylated the fragment could be 60,000 daltons in size. The smaller fragment may not have been resolved on this gel or the antibody may not react with it.

These results are analogous to the form of HGF seen in plasma which is a heterodimeric protein of 82,000 daltons composed of α and β subunits of 51,000 and 26,000 daltons, respectively.

A full-length human L5/3 cDNA was then constructed. Since the longest human L5/3 cDNA was not full-length and was missing 16 bp from the 5' end (Sequence ID No. 1), a full-length L5/3 cDNA was constructed by addition of adaptors. The following complementary oligonucleotides were synthesized: coding: 5' GCGAATTCCACC ATGGGGTGGCTCCCA 3' (SEQ ID NO:9) complementary 3' CGCTTAAGGTGGTACCCCACCGAGGGTTTAA 5' (SEQ ID NO:10).

When hybridized to each other this adaptor has the following features: 1) the presence of an Eco RI restriction site (5' GAATTC 3') at the 5' end for cloning into the Eco RI sites in expression vectors; 2) a Kozak consensus sequence surrounding the ATG coding for the initiator methionine (5' CCACCATGG 3'; Kozak, 1986) to optimize translation from this methionine; 3) an overhanging-end at the 3' end of the adaptor that is compatible with the EcoRI site present at the 5' end of the L5/3cDNA-(33) for ligation together; and 4) after ligation of the adaptor to the cDNA insert the Eco RI sites at the ends of the original cDNA will not be reconstituted and therefore the only Eco RI sites will be due to the adaptor.

The 2200 bp cDNA insert from the human L5/3cDNA-(33) was isolated after digestion with Eco RI (nucleotides 1–2219 in Sequence ID No. 1) and ligated to the hybridized oligonucleotides (adaptor). The resulting mixture was digested with Eco RI and electrophoresed on low melting point agarose. The band representing the cDNA with ligated adaptors was excised and the DNA isolated. This DNA was then ligated to the vector Bluescript SK± (Stratagene, La Jolla, Calif.), and used to transform *E. coli. E. Coli* transformed with the anticipated full-length L5/3cDNA containing plasmid were initially identified by restriction enzyme digestion of plasmid isolated from white colonies on agar plates containing IPTG, X-Gal and ampicillin (*E. coli* containing the recombinant vector will give white colonies while Bluescript without an insert will give blue colonies). Final confirmation of the full-length construct was determined by DNA sequence analysis.

After adaptor ligation to the human L5/3 cDNA insert there are eight nucleotide differences when the sequence is compared to the exons in the gene for human L5/3 (nucleotides 1301–1312 in Sequence ID No. 6). These are due to the original Eco RI site present at the 5' end of the L5/3cDNA insert that is the result of linker addition during the construction of the cDNA library and is not naturally present in the cDNA (as determined from the sequence of the gene for this region). These differences result in three amino acid substitutions that we do not anticipate will affect the function of recombinant full-length L5/3 protein since they are present in the proposed signal peptide. The sequence of the full-length construct is shown in Sequence ID No. 7. Residues 6–8 are Leu-Leu-Leu in the gene coding for human L5/3 (Sequence ID No. 6) and Asn-Ser-Val in the full length L5/3 cDNA (Sequence ID No. 7). Adaptor(s) are also present at the 3' end of the cDNA but should not affect the expression of L5/3 since they are present in the 3' noncoding region of the cDNA.

Mammalian expression vectors were also constructed. The full-length L5/3 insert was isolated from the Bluescript vector after digestion with Eco RI. The insert was then cloned into the Eco RI site of the expression vector pDX. This expression vector was obtained from Dr. Kathy Berkner of Zymogenetics. pDX contains an origin of replication, a SV-40 enhancer, a adenovirus promoter, splice sequences and a polyadenylation signal for appropriate replication and transcription of the inserted cDNA and the accurate synthesis and secretion of the expressed protein. The cDNA provides the signal sequence for secretion. This expression vector has been used to transfect the eukaryotic cell line—Hela which does not normally express L5/3 protein.

Expression in general may be achieved in a variety of host systems including, in particular, mammalian and bacterial systems, as well as yeast based systems. In addition, other cell systems have become available such as the baculovirus vectors used to express protein encoding genes in insect cells. The expression system discussed here is illustrative, and it is understood by those in the art that a variety of expression systems can be used.

Additional factors necessary or helpful in effecting expression may subsequently be identified.

As the nucleotide sequences encoding the human and mouse L5/3 proteins are now available, these may be expressed in a variety of systems. If procaryotic systems are used, an intronless coding sequence should be used, along with suitable control sequences. The cDNA clones for any of the above L5/3 proteins may be excised with suitable restriction enzymes and ligated into procaryotic vectors for such expression. For procaryotic expression of L5/3 genomic DNA, the DNA should be modified to remove the introns, either by sitedirected mutagenesis, or by retrieving corresponding portions of cDNA and substituting them for the intron-containing genomic sequences. The intronless coding DNA is then ligated into expression vectors for procaryotic expression.

As discussed above, L5/3 encoding sequences may also be used directly in an expression system capable of processing the introns, usually a mammalian host cell culture. To effect such expression, the genomic sequences can be ligated downstream from a controllable mammalian promoter which regulates the expression of these sequences in suitable mammalian cells.

E. coli RRI cells carrying the plasmid containing LS/3cDNA (#33) exhibited in Sequence ID No. 1 has been deposited with the American Type Cell Culture in Rockville, Md. and is designated ATCC No. 68976 (deposited on May 6, 1992).

The gene sequence No. 1 submitted below is useful of course when labeled by for example Nick translation as a probe for the D3F15S2 locus on human chromosome 3. This is significant with respect to detection of mutations which provide an indication of one's predisposition to lung carcinoma, renal cell carcinoma and Von Hipple-Lindau syndrome. Further, the protein coded by the DNA and associated cDNA is useful as an in vitro growth promoter particularly for hepatocytes. This can be used to alter growth characteristics of hepatocytes by combining minor amounts (0.1 to 100 nanograms) of the protein per milliliter of growth serum with hepatocytes.

Further the antibody to the L5/3 protein is useful for detection of the L5/3 protein in human serum. This again is useful for the purpose of again detecting any alteration of the chromosome 3 locus D3F15S2 and again an indication of the predisposition towards cancer.

Further, cited below are the DNA sequences for both the human and the mouse along with the cDNA sequences for the human and mouse and the protein associated with the human DNA.

Sequence ID No. 1: cDNA for Human L5/3 clone #33 and associated protein.

Sequence ID No. 2: cDNA for Human L5/3 clone #33 with polymorphism relative to Sequence ID No. 1 and associated protein.

Sequence ID No. 3: cDNA for Human L5/3 clone #19 and associated protein.

Sequence ID No. 4: cDNA for Mouse L5/3 and associated protein.

Sequence ID No. 5: DNA for Mouse L5/3 and associated protein.

Sequence ID No. 6: DNA Sequence of Human L5/3 and associated protein.

Sequence ID No. 7: cDNA Sequence of Human L5/3 with 5' and 3' adaptors added to make a full length cDNA.

Sequence ID No. 8: DNA Sequence human L5/3 depicted in the FIGURE.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i i i) NUMBER OF SEQUENCES: 10

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2219 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: cDNA to mRNA

(i v) ANTI-SENSE: no

(v i) ORIGINAL SOURCE:
(A) ORGANISM: human
(D) DEVELOPMENTAL STAGE: fetal
(F) TISSUE TYPE: liver

(v i i) IMMEDIATE SOURCE:
(A) LIBRARY: cDNA
(B) CLONE: #33

(v i i i) POSITION IN GENOME:
(A) CHROMOSOME/SEGMENT: human 3p21/D3F15S2

(i x) FEATURE:
(C) IDENTIFICATION METHOD: experimental
(D) OTHER INFORMATION: Includes five polymorphisms at the nucleotide level; one of which results in an amino acid substitution (nucleotide 619). Sequence ID NO:2: contains the identical sequence with the other

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polymorphic amino acid.

(x) PUBLICATION INFORMATION:

(K) RELEVANT RESIDUES IN SEQ ID NO: 1: FROM 1 TO 2219

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:1:

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TC  CTG CTG CTT CTG ACT CAA TAC TTA GGG GTC CCT GGG CAG CGC TCG          47
    Leu Leu Leu Leu Thr Gln Tyr Leu Gly Val Pro Gly Gln Arg Ser
                10                  15                  20

CCA TTG AAT GAC TTC CAA GTG CTC CGG GGC ACA GAG CTA CAG CAC CTG          95
Pro Leu Asn Asp Phe Gln Val Leu Arg Gly Thr Glu Leu Gln His Leu
            25                  30                  35

CTA CAT GCG GTG GTG CCC GGG CCT TGG CAG GAG GAT GTG GCA GAT GCT         143
Leu His Ala Val Val Pro Gly Pro Trp Gln Glu Asp Val Ala Asp Ala
        40                  45                  50

GAA GAG TGT GCT GGT CGC TGT GGG CCC TTA ATG GAC TGC CGG GCC TTC         191
Glu Glu Cys Ala Gly Arg Cys Gly Pro Leu Met Asp Cys Arg Ala Phe
    55                  60                  65

CAC TAC AAC GTG AGC AGC CAT GGT TGC CAA CTG CTG CCA TGG ACT CAA         239
His Tyr Asn Val Ser Ser His Gly Cys Gln Leu Leu Pro Trp Thr Gln
70                  75                  80                  85

CAC TCG CCC CAC ACG AGG CTG CGG CGT TCT GGG CGC TGT GAC CTC TTC         287
His Ser Pro His Thr Arg Leu Arg Arg Ser Gly Arg Cys Asp Leu Phe
                90                  95                  100

CAG AAG AAA GAC TAC GTA CGG ACC TGC ATC ATG AAC AAT GGG GTT GGG         335
Gln Lys Lys Asp Tyr Val Arg Thr Cys Ile Met Asn Asn Gly Val Gly
            105                 110                 115

TAC CGG GGC ACC ATG GCC ACG ACC GTG GGT GGC CTG CCC TGC CAG GCT         383
Tyr Arg Gly Thr Met Ala Thr Thr Val Gly Gly Leu Pro Cys Gln Ala
        120                 125                 130

TGG AGC CAC AAG TTC CCG AAT GAT CAC AAG TAC ACG CCC ACT CTC CGG         431
Trp Ser His Lys Phe Pro Asn Asp His Lys Tyr Thr Pro Thr Leu Arg
    135                 140                 145

AAT GGC CTG GAA GAG AAC TTC TGC CGT AAC CCT GAT GGC GAC CCC GGA         479
Asn Gly Leu Glu Glu Asn Phe Cys Arg Asn Pro Asp Gly Asp Pro Gly
150                 155                 160                 165

GGT CCT TGG TGC TAC ACA ACA GAC CCT GCT GTG CGC TTC CAG AGC TGC         527
Gly Pro Trp Cys Tyr Thr Thr Asp Pro Ala Val Arg Phe Gln Ser Cys
                170                 175                 180

GGC ATC AAA TCC TGC CGG GAG GCC GCG TGT GTC TGG TGC AAT GGC GAG         575
Gly Ile Lys Ser Cys Arg Glu Ala Ala Cys Val Trp Cys Asn Gly Glu
            185                 190                 195

GAA TAC CGC GGC GCG GTA GAC CGC ACG GAG TCA GGG CGC GAG TGC CAG         623
Glu Tyr Arg Gly Ala Val Asp Arg Thr Glu Ser Gly Arg Glu Cys Gln
        200                 205                 210

CGC TGG GAT CTT CAG CAC CCG CAC CAG CAC CCC TTC GAG CCG GGC AAG         671
Arg Trp Asp Leu Gln His Pro His Gln His Pro Phe Glu Pro Gly Lys
    215                 220                 225

TTC CTC GAC CAA GGT CTG GAC GAC AAC TAT TGC CGG AAT CCT GAC GGC         719
Phe Leu Asp Gln Gly Leu Asp Asp Asn Tyr Cys Arg Asn Pro Asp Gly
230                 235                 240                 245

TCC GAG CGG CCA TGG TGC TAC ACT ACG GAT CCG CAG ATC GAG CGA GAG         767
Ser Glu Arg Pro Trp Cys Tyr Thr Thr Asp Pro Gln Ile Glu Arg Glu
                250                 255                 260

TTC TGT GAC CTC CCC CGC TGC GGG TCC GAG GCA CAG CCC CGC CAA GAG         815
Phe Cys Asp Leu Pro Arg Cys Gly Ser Glu Ala Gln Pro Arg Gln Glu
            265                 270                 275

GCC ACA ACT GTC AGC TGC TTC CGC GGG AAG GGT GAG GGC TAC CGG GGC         863
Ala Thr Thr Val Ser Cys Phe Arg Gly Lys Gly Glu Gly Tyr Arg Gly
        280                 285                 290

ACA GCC AAT ACC ACC ACT GCG GGC GTA CCT TGC CAG CGT TGG GAC GCG         911
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Thr Ala Asn Thr Thr Thr Ala Gly Val Pro Cys Gln Arg Trp Asp Ala
    295                 300                 305

CAA ATC CCT CAT CAG CAC CGA TTT ACG CCA GAA AAA TAC GCG TGC AAA      959
Gln Ile Pro His Gln His Arg Phe Thr Pro Glu Lys Tyr Ala Cys Lys
310                 315                 320                 325

GAC CTT CGG GAG AAC TTC TGC CGG AAC CCC GAC GGC TCA GAG GCG CCC     1007
Asp Leu Arg Glu Asn Phe Cys Arg Asn Pro Asp Gly Ser Glu Ala Pro
                330                 335                 340

TGG TGC TTC ACA CTG CGG CCC GGC ATG CGC GCG GCC TTT TGC TAC CAG     1055
Trp Cys Phe Thr Leu Arg Pro Gly Met Arg Ala Ala Phe Cys Tyr Gln
            345                 350                 355

ATC CGG CGT TGT ACA GAC GAC GTG CGG CCC CAG GAC TGC TAC CAC GGC     1103
Ile Arg Arg Cys Thr Asp Asp Val Arg Pro Gln Asp Cys Tyr His Gly
        360                 365                 370

GCA GGG GAG CAG TAC CGC GGC ACG GTC AGC AAG ACC CGC AAG GGT GTC     1151
Ala Gly Glu Gln Tyr Arg Gly Thr Val Ser Lys Thr Arg Lys Gly Val
    375                 380                 385

CAG TGC CAG CGC TGG TCC GCT GAG ACG CCG CAC AAG CCG CAG TTC ACG     1199
Gln Cys Gln Arg Trp Ser Ala Glu Thr Pro His Lys Pro Gln Phe Thr
390                 395                 400                 405

TTT ACC TCC GAR CCG CAT GCA CAA CTG GAG GAG AAC TTC TGC CGG AAC     1247
Phe Thr Ser Glu Pro His Ala Gln Leu Glu Glu Asn Phe Cys Arg Asn
                410                 415                 420

CCA GAT GGG GAT AGC CAT GGG CCC TGG TGC TAC ACG ATG GAC CCA AGG     1295
Pro Asp Gly Asp Ser His Gly Pro Trp Cys Tyr Thr Met Asp Pro Arg
            425                 430                 435

ACC CCA TTC GAC TAC TGT GCC CTG CGA CGC TGC GCT GAT GAC CAG CCG     1343
Thr Pro Phe Asp Tyr Cys Ala Leu Arg Arg Cys Ala Asp Asp Gln Pro
        440                 445                 450

CCA TCA ATC CTG GAC CCC CCA GAC CAG GTG CAG TTT GAG AAG TGT GGC     1391
Pro Ser Ile Leu Asp Pro Pro Asp Gln Val Gln Phe Glu Lys Cys Gly
    455                 460                 465

AAG AGG GTG GAT CGG CTG GAT CAG CGG CGT TCC AAG CTG CGC GTG GTT     1439
Lys Arg Val Asp Arg Leu Asp Gln Arg Arg Ser Lys Leu Arg Val Val
470                 475                 480                 485

GGG GGC CAT CCG GGC AAC TCA CCC TGG ACA GTC AGC TTG CGG AAT CGG     1487
Gly Gly His Pro Gly Asn Ser Pro Trp Thr Val Ser Leu Arg Asn Arg
                490                 495                 500

CAG GGC CAG CAT TTC TGC GGG GGG TCT CTA GTG AAG GAG CAG TGG ATA     1535
Gln Gly Gln His Phe Cys Gly Gly Ser Leu Val Lys Glu Gln Trp Ile
            505                 510                 515

CTG ACT GCC CGG CAG TGC TTC TCC TCC TGC CAT ATG CCT CTC ACG GGC     1583
Leu Thr Ala Arg Gln Cys Phe Ser Ser Cys His Met Pro Leu Thr Gly
        520                 525                 530

TAT GAG GTA TGG TTG GGC ACC CTG TTC CAG AAC CCA CAG CAT GGA GAG     1631
Tyr Glu Val Trp Leu Gly Thr Leu Phe Gln Asn Pro Gln His Gly Glu
    535                 540                 545

CCA AGC CTA CAG CGG GTC CCA GTA GCC AAG ATG GTG TGT GGG CCC TCA     1679
Pro Ser Leu Gln Arg Val Pro Val Ala Lys Met Val Cys Gly Pro Ser
550                 555                 560                 565

GGC TCC CAG CTT GTC CTG CTC AAG CTG GAG AGA TCT GTG ACC CTG AAC     1727
Gly Ser Gln Leu Val Leu Leu Lys Leu Glu Arg Ser Val Thr Leu Asn
                570                 575                 580

CAG CGY GTG GCC CTG ATC TGC CTG CCC CCT GAA TGG TAT GTG GTG CCT     1775
Gln Arg Val Ala Leu Ile Cys Leu Pro Pro Glu Trp Tyr Val Val Pro
            585                 590                 595

CCA GGG ACC AAG TGT GAG ATT GCA GGC TGG GGT GAG ACC AAA GGT ACG     1823
Pro Gly Thr Lys Cys Glu Ile Ala Gly Trp Gly Glu Thr Lys Gly Thr
        600                 605                 610

GGT AAT GAC ACA GTC CTA AAT GTG GCC TTG CTG AAT GTC ATC TCC AAC     1871
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Gly Asn Asp Thr Val Leu Asn Val Ala Leu Leu Asn Val Ile Ser Asn
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CAG GAG TGT AAC ATC AAR CAC CGA GGA CGT GTG CGK GAG AGT GAG ATG      1919
Gln Glu Cys Asn Ile Lys His Arg Gly Arg Val Arg Glu Ser Glu Met
630                 635                 640                 645

TGC ACT GAG GGA CTG TTG GCC CCT GTG GGG GCC TGT GAG GGT GAC TAC      1967
Cys Thr Glu Gly Leu Leu Ala Pro Val Gly Ala Cys Glu Gly Asp Tyr
                650                 655                 660

GGG GGC CCA CTT GCC TGC TTT ACC CAC AAC TGC TGG GTC CTG GAA GGA      2015
Gly Gly Pro Leu Ala Cys Phe Thr His Asn Cys Trp Val Leu Glu Gly
            665                 670                 675

ATT ATA ATC CCC AAC CGA GTA TGC GCA AGG TCC CGC TGG CCA GCT GTC      2063
Ile Ile Ile Pro Asn Arg Val Cys Ala Arg Ser Arg Trp Pro Ala Val
        680                 685                 690

TTC ACG CGT GTC TCT GTG TTT GTG GAC TGG ATT CAC AAG GTC ATG AGA      2111
Phe Thr Arg Val Ser Val Phe Val Asp Trp Ile His Lys Val Met Arg
    695                 700                 705

CTG GGT TAGGCCCAGC CTTGATGCCA TATGCCTTGG GGAGGACAAA ACTTCTTGTC      2167
Leu Gly
710

AGACATAAAG CCATGTTTCC TCTTTATGCC TGTAAAAAAA AAAAAAAAAA AA           2219
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(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2219 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: cDNA to mRNA

(i v) ANTI-SENSE: no

(v i) ORIGINAL SOURCE:
(A) ORGANISM: human
(D) DEVELOPMENTAL STAGE: fetal
(F) TISSUE TYPE: liver

(v i i) IMMEDIATE SOURCE:
(A) LIBRARY: cDNA
(B) CLONE: #33

(v i i i) POSITION IN GENOME:
(A) CHROMOSOME/SEGMENT: human 3p21/D3F15S2

(i x) FEATURE:
(C) IDENTIFICATION METHOD: experimental
(D) OTHER INFORMATION: Includes five polymorphisms at the nucleotide level; one of which results in an amino acid substitution (nucleotide 619). Sequence ID NO:1: contains the identical sequence with the other polymorphic amino acid.

(x) PUBLICATION INFORMATION:
(K) RELEVANT RESIDUES IN SEQ ID NO: 2: FROM 1 TO 2219

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:2:

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TC CTG CTG CTT CTG ACT CAA TAC TTA GGG GTC CCT GGG CAG CGC TCG        47
   Leu Leu Leu Leu Thr Gln Tyr Leu Gly Val Pro Gly Gln Arg Ser
                10                  15                  20

CCA TTG AAT GAC TTC CAA GTG CTC CGG GGC ACA GAG CTA CAG CAC CTG      95
Pro Leu Asn Asp Phe Gln Val Leu Arg Gly Thr Glu Leu Gln His Leu
            25                  30                  35

CTA CAT GCG GTG GTG CCC GGG CCT TGG CAG GAG GAT GTG GCA GAT GCT     143
Leu His Ala Val Val Pro Gly Pro Trp Gln Glu Asp Val Ala Asp Ala
        40                  45                  50

GAA GAG TGT GCT GGT CGC TGT GGG CCC TTA ATG GAC TGC CGG GCC TTC     191
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Glu Glu Cys Ala Gly Arg Cys Gly Pro Leu Met Asp Cys Arg Ala Phe
    55                  60                  65

CAC TAC AAC GTG AGC AGC CAT GGT TGC CAA CTG CTG CCA TGG ACT CAA      239
His Tyr Asn Val Ser Ser His Gly Cys Gln Leu Leu Pro Trp Thr Gln
 70                  75                  80                  85

CAC TCG CCC CAC ACG AGG CTG CGG CGT TCT GGG CGC TGT GAC CTC TTC      287
His Ser Pro His Thr Arg Leu Arg Arg Ser Gly Arg Cys Asp Leu Phe
                90                  95                 100

CAG AAG AAA GAC TAC GTA CGG ACC TGC ATC ATG AAC AAT GGG GTT GGG      335
Gln Lys Lys Asp Tyr Val Arg Thr Cys Ile Met Asn Asn Gly Val Gly
            105                 110                 115

TAC CGG GGC ACC ATG GCC ACG ACC GTG GGT GGC CTG CCC TGC CAG GCT      383
Tyr Arg Gly Thr Met Ala Thr Thr Val Gly Gly Leu Pro Cys Gln Ala
        120                 125                 130

TGG AGC CAC AAG TTC CCG AAT GAT CAC AAG TAC ACG CCC ACT CTC CGG      431
Trp Ser His Lys Phe Pro Asn Asp His Lys Tyr Thr Pro Thr Leu Arg
    135                 140                 145

AAT GGC CTG GAA GAG AAC TTC TGC CGT AAC CCT GAT GGC GAC CCC GGA      479
Asn Gly Leu Glu Glu Asn Phe Cys Arg Asn Pro Asp Gly Asp Pro Gly
150                 155                 160                 165

GGT CCT TGG TGC TAC ACA ACA GAC CCT GCT GTG CGC TTC CAG AGC TGC      527
Gly Pro Trp Cys Tyr Thr Thr Asp Pro Ala Val Arg Phe Gln Ser Cys
                170                 175                 180

GGC ATC AAA TCC TGC CGG GAG GCC GCG TGT GTC TGG TGC AAT GGC GAG      575
Gly Ile Lys Ser Cys Arg Glu Ala Ala Cys Val Trp Cys Asn Gly Glu
            185                 190                 195

GAA TAC CGC GGC GCG GTA GAC CGC ACG GAG TCA GGG CGC GAG TTC CAG      623
Glu Tyr Arg Gly Ala Val Asp Arg Thr Glu Ser Gly Arg Glu Phe Gln
        200                 205                 210

CGC TGG GAT CTT CAG CAC CCG CAC CAG CAC CCC TTC GAG CCG GGC AAG      671
Arg Trp Asp Leu Gln His Pro His Gln His Pro Phe Glu Pro Gly Lys
    215                 220                 225

TTC CTC GAC CAA GGT CTG GAC GAC AAC TAT TGC CGG AAT CCT GAC GGC      719
Phe Leu Asp Gln Gly Leu Asp Asp Asn Tyr Cys Arg Asn Pro Asp Gly
230                 235                 240                 245

TCC GAG CGG CCA TGG TGC TAC ACT ACG GAT CCG CAG ATC GAG CGA GAG      767
Ser Glu Arg Pro Trp Cys Tyr Thr Thr Asp Pro Gln Ile Glu Arg Glu
                250                 255                 260

TTC TGT GAC CTC CCC CGC TGC GGG TCC GAG GCA CAG CCC CGC CAA GAG      815
Phe Cys Asp Leu Pro Arg Cys Gly Ser Glu Ala Gln Pro Arg Gln Glu
            265                 270                 275

GCC ACA ACT GTC AGC TGC TTC CGC GGG AAG GGT GAG GGC TAC CGG GGC      863
Ala Thr Thr Val Ser Cys Phe Arg Gly Lys Gly Glu Gly Tyr Arg Gly
        280                 285                 290

ACA GCC AAT ACC ACC ACT GCG GGC GTA CCT TGC CAG CGT TGG GAC GCG      911
Thr Ala Asn Thr Thr Thr Ala Gly Val Pro Cys Gln Arg Trp Asp Ala
    295                 300                 305

CAA ATC CCT CAT CAG CAC CGA TTT ACG CCA GAA AAA TAC GCG TGC AAA      959
Gln Ile Pro His Gln His Arg Phe Thr Pro Glu Lys Tyr Ala Cys Lys
310                 315                 320                 325

GAC CTT CGG GAG AAC TTC TGC CGG AAC CCC GAC GGC TCA GAG GCG CCC     1007
Asp Leu Arg Glu Asn Phe Cys Arg Asn Pro Asp Gly Ser Glu Ala Pro
                330                 335                 340

TGG TGC TTC ACA CTG CGG CCC GGC ATG CGC GCG GCC TTT TGC TAC CAG     1055
Trp Cys Phe Thr Leu Arg Pro Gly Met Arg Ala Ala Phe Cys Tyr Gln
            345                 350                 355

ATC CGG CGT TGT ACA GAC GAC GTG CGG CCC CAG GAC TGC TAC CAC GGC     1103
Ile Arg Arg Cys Thr Asp Asp Val Arg Pro Gln Asp Cys Tyr His Gly
        360                 365                 370

GCA GGG GAG CAG TAC CGC GGC ACG GTC AGC AAG ACC CGC AAG GGT GTC     1151
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Ala Gly Glu Gln Tyr Arg Gly Thr Val Ser Lys Thr Arg Lys Gly Val
    375                 380                 385
CAG TGC CAG CGC TGG TCC GCT GAG ACG CCG CAC AAG CCG CAG TTC ACG  1199
Gln Cys Gln Arg Trp Ser Ala Glu Thr Pro His Lys Pro Gln Phe Thr
390                 395                 400                 405
TTT ACC TCC GAR CCG CAT GCA CAA CTG GAG GAG AAC TTC TGC CGG AAC  1247
Phe Thr Ser Glu Pro His Ala Gln Leu Glu Glu Asn Phe Cys Arg Asn
                410                 415                 420
CCA GAT GGG GAT AGC CAT GGG CCC TGG TGC TAC ACG ATG GAC CCA AGG  1295
Pro Asp Gly Asp Ser His Gly Pro Trp Cys Tyr Thr Met Asp Pro Arg
            425                 430                 435
ACC CCA TTC GAC TAC TGT GCC CTG CGA CGC TGC GCT GAT GAC CAG CCG  1343
Thr Pro Phe Asp Tyr Cys Ala Leu Arg Arg Cys Ala Asp Asp Gln Pro
        440                 445                 450
CCA TCA ATC CTG GAC CCC CCA GAC CAG GTG CAG TTT GAG AAG TGT GGC  1391
Pro Ser Ile Leu Asp Pro Pro Asp Gln Val Gln Phe Glu Lys Cys Gly
    455                 460                 465
AAG AGG GTG GAT CGG CTG GAT CAG CGG CGT TCC AAG CTG CGC GTG GTT  1439
Lys Arg Val Asp Arg Leu Asp Gln Arg Arg Ser Lys Leu Arg Val Val
470                 475                 480                 485
GGG GGC CAT CCG GGC AAC TCA CCC TGG ACA GTC AGC TTG CGG AAT CGG  1487
Gly Gly His Pro Gly Asn Ser Pro Trp Thr Val Ser Leu Arg Asn Arg
                490                 495                 500
CAG GGC CAG CAT TTC TGC GGG GGG TCT CTA GTG AAG GAG CAG TGG ATA  1535
Gln Gly Gln His Phe Cys Gly Gly Ser Leu Val Lys Glu Gln Trp Ile
            505                 510                 515
CTG ACT GCC CGG CAG TGC TTC TCC TCC TGC CAT ATG CCT CTC ACG GGC  1583
Leu Thr Ala Arg Gln Cys Phe Ser Ser Cys His Met Pro Leu Thr Gly
        520                 525                 530
TAT GAG GTA TGG TTG GGC ACC CTG TTC CAG AAC CCA CAG CAT GGA GAG  1631
Tyr Glu Val Trp Leu Gly Thr Leu Phe Gln Asn Pro Gln His Gly Glu
    535                 540                 545
CCA AGC CTA CAG CGG GTC CCA GTA GCC AAG ATG GTG TGT GGG CCC TCA  1679
Pro Ser Leu Gln Arg Val Pro Val Ala Lys Met Val Cys Gly Pro Ser
550                 555                 560                 565
GGC TCC CAG CTT GTC CTG CTC AAG CTG GAG AGA TCT GTG ACC CTG AAC  1727
Gly Ser Gln Leu Val Leu Leu Lys Leu Glu Arg Ser Val Thr Leu Asn
                570                 575                 580
CAG CGY GTG GCC CTG ATC TGC CTG CCC CCT GAA TGG TAT GTG GTG CCT  1775
Gln Arg Val Ala Leu Ile Cys Leu Pro Pro Glu Trp Tyr Val Val Pro
            585                 590                 595
CCA GGG ACC AAG TGT GAG ATT GCA GGC TGG GGT GAG ACC AAA GGT ACG  1823
Pro Gly Thr Lys Cys Glu Ile Ala Gly Trp Gly Glu Thr Lys Gly Thr
        600                 605                 610
GGT AAT GAC ACA GTC CTA AAT GTG GCC TTG CTG AAT GTC ATC TCC AAC  1871
Gly Asn Asp Thr Val Leu Asn Val Ala Leu Leu Asn Val Ile Ser Asn
    615                 620                 625
CAG GAG TGT AAC ATC AAR CAC CGA GGA CGT GTG CGK GAG AGT GAG ATG  1919
Gln Glu Cys Asn Ile Lys His Arg Gly Arg Val Arg Glu Ser Glu Met
630                 635                 640                 645
TGC ACT GAG GGA CTG TTG GCC CCT GTG GGG GCC TGT GAG GGT GAC TAC  1967
Cys Thr Glu Gly Leu Leu Ala Pro Val Gly Ala Cys Glu Gly Asp Tyr
                650                 655                 660
GGG GGC CCA CTT GCC TGC TTT ACC CAC AAC TGC TGG GTC CTG GAA GGA  2015
Gly Gly Pro Leu Ala Cys Phe Thr His Asn Cys Trp Val Leu Glu Gly
            665                 670                 675
ATT ATA ATC CCC AAC CGA GTA TGC GCA AGG TCC CGC TGG CCA GCT GTC  2063
Ile Ile Ile Pro Asn Arg Val Cys Ala Arg Ser Arg Trp Pro Ala Val
        680                 685                 690
TTC ACG CGT GTC TCT GTG TTT GTG GAC TGG ATT CAC AAG GTC ATG AGA  2111
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Phe Thr Arg Val Ser Val Phe Val Asp Trp Ile His Lys Val Met Arg
    695                 700                 705

CTG GGT TAGGCCCAGC CTTGATGCCA TATGCCTTGG GGAGGACAAA ACTTCTTGTC      2167
Leu Gly
710

AGACATAAAG CCATGTTTCC TCTTTATGCC TGTAAAAAAA AAAAAAAAAA AA          2219
```

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2021 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: cDNA to mRNA

(i v) ANTI-SENSE: no

(v i) ORIGINAL SOURCE:
(A) ORGANISM: human
(D) DEVELOPMENTAL STAGE: fetal
(F) TISSUE TYPE: liver

(v i i) IMMEDIATE SOURCE:
(A) LIBRARY: cDNA
(B) CLONE: #19

(v i i i) POSITION IN GENOME:
(A) CHROMOSOME/SEGMENT: human 3p21/D3F15S2

(i x) FEATURE:
(C) IDENTIFICATION METHOD: experimental
(D) OTHER INFORMATION: This sequence is a variant where two regions were found to be deleted when compared to SEQ ID NO:1.

(x) PUBLICATION INFORMATION:
(K) RELEVANT RESIDUES IN SEQ ID NO:3: FROM 1 TO 2021

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:3:

```
A TGC TTA GGG GTC CCT GGG CAG CGC TCG CCA TTG AAT GAC TTC CAA          46
  Cys Leu Gly Val Pro Gly Gln Arg Ser Pro Leu Asn Asp Phe Gln
          15                  20                  25

GTG CTC CGG GGC ACA GAG CTA CAG CAC CTG CTA CAT GCG GTG GTG CCC        94
Val Leu Arg Gly Thr Glu Leu Gln His Leu Leu His Ala Val Val Pro
        30                  35                  40

GGG CCT TGG CAG GAG GAT GTG GCA GAT GCT GAA GAG TGT GCT GGT CGC       142
Gly Pro Trp Gln Glu Asp Val Ala Asp Ala Glu Glu Cys Ala Gly Arg
    45                  50                  55

TGT GGG CCC TTA ATG GAC TGC CGG GCC TTC CAC TAC AAC GTG AGC AGC       190
Cys Gly Pro Leu Met Asp Cys Arg Ala Phe His Tyr Asn Val Ser Ser
60                  65                  70                  75

CAT GGT TGC CAA CTG CTG CCA TGG ACT CAA CAC TCG CCC CAC ACG AGG       238
His Gly Cys Gln Leu Leu Pro Trp Thr Gln His Ser Pro His Thr Arg
                80                  85                  90

CTG CGG CGT TCT GGG CGC TGT GAC CTC TTC CAG AAG AAA GAC TAC GTA       286
Leu Arg Arg Ser Gly Arg Cys Asp Leu Phe Gln Lys Lys Asp Tyr Val
            95                  100                 105

CGG ACC TGC ATC ATG AAC AAT GGG GTT GGG TAC CGG GGC ACC ATG GCC       334
Arg Thr Cys Ile Met Asn Asn Gly Val Gly Tyr Arg Gly Thr Met Ala
        110                 115                 120

ACG ACC GTG GGT GGC CTG CCC TGC CAG GCT TGG AGC CAC AAG TTC CCG       382
Thr Thr Val Gly Gly Leu Pro Cys Gln Ala Trp Ser His Lys Phe Pro
    125                 130                 135

AAT GAT CAC AAG TAC ACG CCC ACT CTC CGG AAT GGC CTG GAA GAG AAC       430
Asn Asp His Lys Tyr Thr Pro Thr Leu Arg Asn Gly Leu Glu Glu Asn
140                 145                 150                 155
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TTC TGC CGT AAC CCT GAT GGC GAC CCC GGA GGT CCT TGG TGC TAC ACA          478
Phe Cys Arg Asn Pro Asp Gly Asp Pro Gly Gly Pro Trp Cys Tyr Thr
                160                 165                 170

ACA GAC CCT GCT GTG CGC TTC CAG AGC TGC GGC ATC AAA TCC TGC CGG          526
Thr Asp Pro Ala Val Arg Phe Gln Ser Cys Gly Ile Lys Ser Cys Arg
            175                 180                 185

GAG GCC GCG TGT GTC TGG TGC AAT GGC GAG GAA TAC CGC GGC GCG GTA          574
Glu Ala Ala Cys Val Trp Cys Asn Gly Glu Glu Tyr Arg Gly Ala Val
        190                 195                 200

GAC CGC ACG GAG TCA GGG CGC GAG TGC CAG CGC TGG GAT CTT CAG CAC          622
Asp Arg Thr Glu Ser Gly Arg Glu Cys Gln Arg Trp Asp Leu Gln His
    205                 210                 215

CCG CAC CAG CAC CCC TTC GAG CCG GGC AAG TTC CTC GAC CAA GGT CTG          670
Pro His Gln His Pro Phe Glu Pro Gly Lys Phe Leu Asp Gln Gly Leu
220                 225                 230                 235

GAC GAC AAC TAT TGC CGG AAT CCT GAC GGC TCC GAG CGG CCA TGG TGC          718
Asp Asp Asn Tyr Cys Arg Asn Pro Asp Gly Ser Glu Arg Pro Trp Cys
                240                 245                 250

TAC ACT ACG GAT CCG CAG ATC GAG CGA GAG TTC TGT GAC CTC CCC CGC          766
Tyr Thr Thr Asp Pro Gln Ile Glu Arg Glu Phe Cys Asp Leu Pro Arg
            255                 260                 265

TGC GGG TCC GAG GCA CAG CCC CGC CAA GAG GCC ACA ACT GTC AGC TGC          814
Cys Gly Ser Glu Ala Gln Pro Arg Gln Glu Ala Thr Thr Val Ser Cys
        270                 275                 280

TTC CGC GGG AAG GGT GAG GGC TAC CGG GGC ACA GCC AAT ACC ACC ACT          862
Phe Arg Gly Lys Gly Glu Gly Tyr Arg Gly Thr Ala Asn Thr Thr Thr
    285                 290                 295

GCG GGC GTA CCT TGC CAG CGT TGG GAC GCG CAA ATC CCT CAT CAG CAC          910
Ala Gly Val Pro Cys Gln Arg Trp Asp Ala Gln Ile Pro His Gln His
300                 305                 310                 315

CGA TTT ACG CCA GAA AAA TAC GCG TGC AAA GAC CTT CGG GAG AAC TTC          958
Arg Phe Thr Pro Glu Lys Tyr Ala Cys Lys Asp Leu Arg Glu Asn Phe
                320                 325                 330

TGC CGG AAC CCC GAC GGC TCA GAG GCG CCC TGG TGC TTC ACA CTG CGG         1006
Cys Arg Asn Pro Asp Gly Ser Glu Ala Pro Trp Cys Phe Thr Leu Arg
            335                 340                 345

CCC GGC ATG CGC GCG GCC TTT TGC TAC CAG ATC CGG CGT TGT ACA GAC         1054
Pro Gly Met Arg Ala Ala Phe Cys Tyr Gln Ile Arg Arg Cys Thr Asp
        350                 355                 360

GAC GTG CGG CCC CAG GAC TGC TAC CAC GGC GCA GGG GAG CAG TAC CGC         1102
Asp Val Arg Pro Gln Asp Cys Tyr His Gly Ala Gly Glu Gln Tyr Arg
    365                 370                 375

GGC ACG GTC AGC AAG ACC CGC AAG GGT GTC CAG TGC CAG CGC TGG TCC         1150
Gly Thr Val Ser Lys Thr Arg Lys Gly Val Gln Cys Gln Arg Trp Ser
380                 385                 390                 395

GCT GAG ACG CCG CAC AAG CCG CAG TTC ACG TTT ACC TCC GAA CCG CAT         1198
Ala Glu Thr Pro His Lys Pro Gln Phe Thr Phe Thr Ser Glu Pro His
                400                 405                 410

GCA CAA CTG GAG GAG AAC TTC TGC CGG AAC CCA GAT GGG GAT AGC CAT         1246
Ala Gln Leu Glu Glu Asn Phe Cys Arg Asn Pro Asp Gly Asp Ser His
            415                 420                 425

GGG CCC TGG TGC TAC ACG ATG GAC CCA AGG ACC CCA TTC GAC TAC TGT         1294
Gly Pro Trp Cys Tyr Thr Met Asp Pro Arg Thr Pro Phe Asp Tyr Cys
        430                 435                 440

GCC CTG CGA CGC TGC GCT GAT GAC CAG CCG CCA TCA ATC CTG GAC CCC         1342
Ala Leu Arg Arg Cys Ala Asp Asp Gln Pro Pro Ser Ile Leu Asp Pro
    445                 450                 455

CCA GGC AGG GCC AGC ATT TCT GCG GGG GGT CTC TAGTGAAGGA GCAGTGGATA       1395
Pro Gly Arg Ala Ser Ile Ser Ala Gly Gly Leu
460                 465                 470
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CTGACTGCCC GGCAGTGCTT CTCCTCCTGA ACCCACAGCA TGGAGAGCCA AGCCTACAGC    1455
GGGTCCCAGT AGCCAAGATG GTGTGTGGGC CCTCAGGCTC CCAGCTTGTC CTGCTCAAGC    1515
TGGAGAGATC TGTGACCCTG AACCAGCGCG TGGCCCTGAT CTGCCTGCCC CCTGAATGGT    1575
ATGTGGTGCC TCCAGGGACC AAGTGTGAGA TTGCAGGCTG GGGTGAGACC AAAGGTACGG    1635
GTAATGACAC AGTCCTAAAT GTGGCCTTGC TGAATGTCAT CTCCAACCAG GAGTGTAACA    1695
TCAAGCACCG AGGACGTGTG CGTGAGAGTG AGATGTGCAC TGAGGGACTG TTGGCCCCTG    1755
TGGGGGCCTG TGAGGGTGAC TACGGGGGCC CACTTGCCTG CTTTACCCAC AACTGCTGGG    1815
TCCTGGAAGG AATTATAATC CCCAACCGAG TATGCGCAAG GTCCCGCTGG CCAGCTGTCT    1875
TCACGCGTGT CTCTGTGTTT GTGGACTGGA TTCACAAGGT CATGAGACTG GGTTAGGCCC    1935
AGCCTTGATG CCATATGCCT TGGGGAGGAC AAAACTTCTT GTCAGACATA AAGCCATGTT    1995
TCCTCTTTAA AAAAAAAAAA AAAAAA                                         2021
```

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2188 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: cDNA to mRNA

(i v) ANTI-SENSE: no

(v i) ORIGINAL SOURCE:
(A) ORGANISM: mouse
(B) STRAIN: C57BL/6
(D) DEVELOPMENTAL STAGE: adult
(F) TISSUE TYPE: liver

(v i i) IMMEDIATE SOURCE:
(A) LIBRARY: cDNA
(B) CLONE: ML5-2

(v i i i) POSITION IN GENOME:
(A) CHROMOSOME/SEGMENT: mouse 9, Hgfl locus
(B) MAP POSITION: Trf-Gnai-2-Hgfl- Cck

(i x) FEATURE:
(C) IDENTIFICATION METHOD: experimental

(x) PUBLICATION INFORMATION:
(K) RELEVANT RESIDUES IN SEQ ID NO: 4: 1 TO 2188

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:4:

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G GCT CTT GGG CCG CGC TCA CCA CTG AAT GAC TTC CAG CTG TTC CGG          46
  Ala Leu Gly Pro Arg Ser Pro Leu Asn Asp Phe Gln Leu Phe Arg
                  20                  25                  30

GGC ACA GAG TTA AGG AAC CTG TTA CAC ACA GCG GTG CCG GGG CCA TGG        94
Gly Thr Glu Leu Arg Asn Leu Leu His Thr Ala Val Pro Gly Pro Trp
              35                  40                  45

CAG GAG GAT GTG GCA GAT GCT GAG GAG TGT GCT AGG CGC TGT GGG CCC       142
Gln Glu Asp Val Ala Asp Ala Glu Glu Cys Ala Arg Arg Cys Gly Pro
          50                  55                  60

CTT CTG GAC TGT CGG GCC TTC CAC TAC AAC ATG AGC AGC CAT GGT TGC       190
Leu Leu Asp Cys Arg Ala Phe His Tyr Asn Met Ser Ser His Gly Cys
      65                  70                  75

CAG CTG CTG CCG TGG ACC CAG CAC TCG CTG CAC ACA CAG CTA TAC CAC       238
Gln Leu Leu Pro Trp Thr Gln His Ser Leu His Thr Gln Leu Tyr His
  80                  85                  90

TCG AGT CTG TGC CAT CTC TTC CAG AAG AAA GAT TAT GTG CGG ACC TGC       286
Ser Ser Leu Cys His Leu Phe Gln Lys Lys Asp Tyr Val Arg Thr Cys
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95                  100                 105                 110

ATT ATG GAC AAT GGG GTC AGC TAC CGG GGC ACT GTG GCC AGG ACA GCT     334
Ile Met Asp Asn Gly Val Ser Tyr Arg Gly Thr Val Ala Arg Thr Ala
                115                 120                 125

GGT GGC CTG CCC TGC CAA GCC TGG AGT CGC AGG TTC CCC AAT GAC CAC     382
Gly Gly Leu Pro Cys Gln Ala Trp Ser Arg Arg Phe Pro Asn Asp His
            130                 135                 140

AAG TAT ACG CCC ACG CCA AAG AAT GGC CTG GAA GAG AAC TTC TGT AGG     430
Lys Tyr Thr Pro Thr Pro Lys Asn Gly Leu Glu Glu Asn Phe Cys Arg
        145                 150                 155

AAC CCT GAT GGG GAT CCC AGA GGT CCC TGG TGC TAC ACA ACA AAC CGC     478
Asn Pro Asp Gly Asp Pro Arg Gly Pro Trp Cys Tyr Thr Thr Asn Arg
    160                 165                 170

AGT GTG CGT TTC CAG AGC TGT GGC ATC AAA ACC TGC AGG GAG GCT GTT     526
Ser Val Arg Phe Gln Ser Cys Gly Ile Lys Thr Cys Arg Glu Ala Val
175                 180                 185                 190

TGT GTT CTG TGC AAC GGT GAG GAT TAC CGT GGC GAG GTA GAC GTT ACA     574
Cys Val Leu Cys Asn Gly Glu Asp Tyr Arg Gly Glu Val Asp Val Thr
                195                 200                 205

GAG TCA GGG CGG GAG TGT CAA CGC TGG GAC CTG CAG CAC CCC CAC TCG     622
Glu Ser Gly Arg Glu Cys Gln Arg Trp Asp Leu Gln His Pro His Ser
            210                 215                 220

CAC CCT TTC CAG CCT GAA AAG TTC CTA GAC AAA GAT CTG AAA GAC AAC     670
His Pro Phe Gln Pro Glu Lys Phe Leu Asp Lys Asp Leu Lys Asp Asn
        225                 230                 235

TAT TGT CGT AAT CCG GAC GGA TCT GAG CGG CCC TGG TGC TAC ACC ACA     718
Tyr Cys Arg Asn Pro Asp Gly Ser Glu Arg Pro Trp Cys Tyr Thr Thr
    240                 245                 250

GAC CCG AAT GTT GAG CGA GAA TTC TGC GAC CTG CCC AGT TGC GGG CCT     766
Asp Pro Asn Val Glu Arg Glu Phe Cys Asp Leu Pro Ser Cys Gly Pro
255                 260                 265                 270

AAC CTG CCT CCG ACC GTC AAA GGA TCC AAG TCA CAG CGG CGC AAC AAG     814
Asn Leu Pro Pro Thr Val Lys Gly Ser Lys Ser Gln Arg Arg Asn Lys
                275                 280                 285

GGC AAG GCT CTT AAC TGC TTC CGC GGA AAA GGT GAA GAC TAT CGA GGC     862
Gly Lys Ala Leu Asn Cys Phe Arg Gly Lys Gly Glu Asp Tyr Arg Gly
            290                 295                 300

ACA ACC AAT ACC ACC TCT GCG GGC GTG CCC TGC CAG CGG TGG GAT GCG     910
Thr Thr Asn Thr Thr Ser Ala Gly Val Pro Cys Gln Arg Trp Asp Ala
        305                 310                 315

CAG AGT CCA CAC CAG CAC CGC TTT GTG CCA GAG AAA TAT GCT TGC AAG     958
Gln Ser Pro His Gln His Arg Phe Val Pro Glu Lys Tyr Ala Cys Lys
    320                 325                 330

GAC CTT CGT GAG AAT TTC TGC CGG AAT CCT GAT GGC TCC GAG GCG CCT    1006
Asp Leu Arg Glu Asn Phe Cys Arg Asn Pro Asp Gly Ser Glu Ala Pro
335                 340                 345                 350

TGG TGC TTC ACA TCT CGA CCT GGT TTG CGC ATG GCC TTC TGC CAC CAG    1054
Trp Cys Phe Thr Ser Arg Pro Gly Leu Arg Met Ala Phe Cys His Gln
                355                 360                 365

ATC CCA CGC TGC ACT GAA GAA CTG GTG CCA GAG GGA TGC TAC CAC GGC    1102
Ile Pro Arg Cys Thr Glu Glu Leu Val Pro Glu Gly Cys Tyr His Gly
            370                 375                 380

TCA GGT GAA CAG TAT CGT GGC TCA GTC AGC AAG ACG CGC AAG GGC GTT    1150
Ser Gly Glu Gln Tyr Arg Gly Ser Val Ser Lys Thr Arg Lys Gly Val
        385                 390                 395

CAG TGC CAG CAC TGG TCC TCT GAG ACA CCG CAC AAG CCA CAA TTT ACA    1198
Gln Cys Gln His Trp Ser Ser Glu Thr Pro His Lys Pro Gln Phe Thr
    400                 405                 410

CCC ACC TCG GCA CCG CAG GCG GGA CTG GAG GCC AAC TTC TGC AGG AAT    1246
Pro Thr Ser Ala Pro Gln Ala Gly Leu Glu Ala Asn Phe Cys Arg Asn
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415                 420                 425                 430

CCT GAT GGG GAT AGC CAT GGG CCC TGG TGC TAT ACC TTG GAC CCG GAT      1294
Pro Asp Gly Asp Ser His Gly Pro Trp Cys Tyr Thr Leu Asp Pro Asp
                435                 440                 445

ATC CTG TTT GAC TAC TGT GCC CTA CAG CGC TGT GAT GAT GAC CAG CCA      1342
Ile Leu Phe Asp Tyr Cys Ala Leu Gln Arg Cys Asp Asp Asp Gln Pro
            450                 455                 460

CCA TCC ATT CTG GAC CCC CCA GAC CAG GTG GTG TTT GAA AAG TGT GGC      1390
Pro Ser Ile Leu Asp Pro Pro Asp Gln Val Val Phe Glu Lys Cys Gly
        465                 470                 475

AAG AGA GTT GAC AAG AGT AAT AAA CTT CGT GTG GTG GGA GGC CAT CCT      1438
Lys Arg Val Asp Lys Ser Asn Lys Leu Arg Val Val Gly Gly His Pro
    480                 485                 490

GGG AAC TCC CCA TGG ACG GTC AGC TTG CGG AAT CGA CAG GGC CAG CAT      1486
Gly Asn Ser Pro Trp Thr Val Ser Leu Arg Asn Arg Gln Gly Gln His
495                 500                 505                 510

TTC TGT GGG GGC TCC CTA GTG AAG GAG CAG TGG GTA CTG ACT GCC CGG      1534
Phe Cys Gly Gly Ser Leu Val Lys Glu Gln Trp Val Leu Thr Ala Arg
                515                 520                 525

CAA TGC ATC TGG TCA TGC CAC GAA CCT CTC ACA GGA TAC GAG GTA TGG      1582
Gln Cys Ile Trp Ser Cys His Glu Pro Leu Thr Gly Tyr Glu Val Trp
            530                 535                 540

TTG GGT ACA ATT AAC CAG AAC CCA CAG CCT GGA GAG GCA AAC CTG CAG      1630
Leu Gly Thr Ile Asn Gln Asn Pro Gln Pro Gly Glu Ala Asn Leu Gln
        545                 550                 555

AGG GTC CCA GTG GCC AAG GCA GTG TGC GGC CCT GCA GGC TCC CAG CTT      1678
Arg Val Pro Val Ala Lys Ala Val Cys Gly Pro Ala Gly Ser Gln Leu
    560                 565                 570

GTT CTG CTC AAG CTG GAG AGA CCT GTG ATC CTG AAC CAT CAC GTG GCC      1726
Val Leu Leu Lys Leu Glu Arg Pro Val Ile Leu Asn His His Val Ala
575                 580                 585                 590

CTG ATT TGC CTG CCT CCT GAA CAG TAT GTG GTA CCT CCA GGG ACC AAG      1774
Leu Ile Cys Leu Pro Pro Glu Gln Tyr Val Val Pro Pro Gly Thr Lys
                595                 600                 605

TGT GAG ATC GCA GGC TGG GGT GAA TCC ATC GGT ACA AGC AAT AAC ACA      1822
Cys Glu Ile Ala Gly Trp Gly Glu Ser Ile Gly Thr Ser Asn Asn Thr
            610                 615                 620

GTC CTT CAT GTG GCC TCG ATG AAT GTC ATC TCC AAC CAG GAA TGT AAC      1870
Val Leu His Val Ala Ser Met Asn Val Ile Ser Asn Gln Glu Cys Asn
        625                 630                 635

ACG AAG TAC CGA GGA CAC ATA CAA GAG AGT GAG ATA TGC ACC CAG GGA      1918
Thr Lys Tyr Arg Gly His Ile Gln Glu Ser Glu Ile Cys Thr Gln Gly
    640                 645                 650

CTG GTG GTC CCT GTG GGG GCT TGT GAG GGT GAC TAC GGG GGC CCA CTT      1966
Leu Val Val Pro Val Gly Ala Cys Glu Gly Asp Tyr Gly Gly Pro Leu
655                 660                 665                 670

GCC TGC TAT ACC CAT GAC TGC TGG GTC CTA CAG GGA CTT ATC ATC CCG      2014
Ala Cys Tyr Thr His Asp Cys Trp Val Leu Gln Gly Leu Ile Ile Pro
                675                 680                 685

AAC AGA GTG TGT GCA CGG CCC CGC TGG CCA GCT ATC TTC ACA CGG GTG      2062
Asn Arg Val Cys Ala Arg Pro Arg Trp Pro Ala Ile Phe Thr Arg Val
            690                 695                 700

TCT GTG TTC GTG GAC TGG ATT AAC AAG GTC ATG CAG CTG GAG              2104
Ser Val Phe Val Asp Trp Ile Asn Lys Val Met Gln Leu Glu
        705                 710                 715

TAGGCCTGCT TTTGAGCCCT TAGAGATGTC AAGACTTCTC AAACATAAAG CGGCCTTTTC    2164

TCTCTGTCAA AAAAAAAAAA AAAA                                           2188
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(2) INFORMATION FOR SEQ ID NO:5:

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(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6751 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: genomic DNA

(i v) ANTI-SENSE: no

(v i) ORIGINAL SOURCE:
(A) ORGANISM: mouse
(B) STRAIN: Balb/c
(D) DEVELOPMENTAL STAGE: adult
(F) TISSUE TYPE: liver

(v i i) IMMEDIATE SOURCE:
(A) LIBRARY: genomic
(B) CLONE: MGL5-12

(v i i i) POSITION IN GENOME:
(A) CHROMOSOME/SEGMENT: mouse 9, Hgfl locus
(B) MAP POSITION: Trf-Gnai-2-Hgfl- Cck

(i x) FEATURE:
(C) IDENTIFICATION METHOD: experimental

(x) PUBLICATION INFORMATION:
(K) RELEVANT RESIDUES IN SEQ ID NO: 5: 1 TO 6751

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:5:

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AGATCTGATC GGCCAGGGGC TCGAGGGGAG TCACCGAACC CGCCCGGCTC ATAGCCAGGC      60

CGCCTCTCAC TCACCCCCGG CCTCAGCCTC CGCGACCGGC TCACAACATC CGCCCAGCTT     120

TTCGGCTACG GCACCCGTCC AGGCCAAACC GCGTGCTCGC TCGAGCGCTG CTCCAGCCGC     180

GCACGCGCAT ATGCACAGAC CGCAACAGGC TGGCAGAAAA CCCTCCTCCG TCTCCTACCA     240

AGGTGTTTAC CCGTTTTGCC TGATGGTCCA CCTGTTTCGC CCCCACCTTT CCTAGCCCAG     300

CCGTAGCAGG GACTATGTTC TAATCGGTCC CTAGGTCCAC CTGTCTTAAC TCCTACCTTG     360

CCTGGAGGAG GCCTGACCCA CATGCAGCCT GAAAGACCAC TTCTGACAGC AGATTTGCTA     420

CCTGTCACAG CCGCGCACGC CCCCTCCAGA TGGTCATTGA CACCAGATCC AATGGGCAGG     480

GTTGCTTAGC TTACCCTGGT TTGACACTTC TGAGGGGCGA TGGGATGGAT GCTCCTCGGA     540

TGTGCTGCTA GGGGTGTAGG CTGACTGCCC TACAGCTGGG ACTCAGCTGA TAAGGCAGCT     600

TGAACAGGGA GAGGCAGCAT TGGGACTGGG GAAATTGCAG TCCTCACTTT ACAAGAAGAA     660

ACTGAGGCCC AGAAAAAGTAT AATCCAGGGG TCTGGGAAAT CTTGGCAACT CCTGTATAGC     720

AGAGTCTTTT GGCATAGAAG TGTCAGTGGT GATGGCAGCC ACTGTGGTCA CTAGACTCTT     780

GACATGTGAC CCGTGTAACT GAAAATTTCA GTTTTTCACT TTGTAAATCG TAATCACATA     840

GAGTCTGACT ACTGTGATGG GTACCACACC TCTACAGTAA AGCAGGCACC AGGGACTCCA     900

TGCAACTTCT GGAGCGCGTG TAGCAACAGC ATGCGACCTC AGGGATAGAT GGTGGCAGGA     960

AGACAGTGGA GTGATCTTGG CAAGTCTGGG GATTGCATAG AGTAGACGGG CTCTGCCTCA    1020

GGGACACCTA ACGTTTCCAC ACAGAACCCT CCTAAGTCCT GCCTACCACA CAGAGAGGCC    1080

TCTCAGGATC CAGCTGCAAT GAGACAGCAC TCGAGGGCCT CAAACCTAGG CTCCACCTAG    1140

CAACTGTCAC CCTATGTGTC AGTCAAGTCC AGGCAGGTTC AGAGAGGGGG TGTGGAGCCA    1200

GAGTCACCCA ATCCTGAAGG GACAGATTTC ACCATTTCCG GGATGGGGCT GTGGTGGGTC    1260

ACCGTGCAGC CTCCAGCTTA GGAGA ATG GGG TGG CTC CCA CTT CTG CTG CTT       1312
                           Met Gly Trp Leu Pro Leu Leu Leu Leu
                                                5

CTG GTA CAG TGT TCA AGG GCT CTT G GTGAGTGTCA CCCACCCTGA TCCCAGTCTG    1367
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Leu Val Gln Cys Ser Arg Ala Leu G
 10                  15

CCTTCACGAG GGAGTTCACC CCTGGTCTAC ATAGCTATTC TCATTGAGAG TTTACTTTTC   1427

TTTGGGTCCG GGATCAGTGA CCTTGGCCTG TTGAGCAGAG CTGAGAAGGC CTGGGAATTC   1487

AAATACACAC AGTCTGATCA GGACTACATT AGAGCATACT GTAGCCCAGA GGCAGTCTTT   1547

CAACCAGAGA AACTATCCAA CCCAGAAGGC AGGGCTCCTA AGCCCGATGC ACCACTGTAA   1607

CTTATGCCTT TATTCTGGTG AGAGGCCAGA CTTGGGGCCT TCCCCAGGAA GTGTCCAAGC   1667

ATTCTCATCT GAGGGGTGAG AAGGGGCAAG TGTCACAAGG CCAACACACT GTCACCCAAA   1727

TTCTCATGGA GTGGATGTGG TAGACCAGAG CCCAGTGCCA GGTCTCCTAG CAGATGGGCA   1787

ATAATCACTG TATCTGGGCC TCCCCAGCTC ACTGGCATGA AGGGACTTGC TGGGCCCTTG   1847

AAAATATACA TAAGGCCTGC CCCAAAGACC TTGTATTAGA TTCCCTAAAT GAACAAAAGA   1907

TAGGGTGTGT TAAAGTACTA ATGCGCTCAT GCTCACCACG CAG GG CAG CGC TCA       1961
                                                 ly Gln Arg Ser
                                                    20

CCA CTG AAT GAC TTC CAG CTG TTC CGG GGC ACA GAG TTA AGG AAC CTG      2009
Pro Leu Asn Asp Phe Gln Leu Phe Arg Gly Thr Glu Leu Arg Asn Leu
            25                  30                  35

TTA CAC ACA GCG GTG CCG GGG CCA TGG CAG GAG GAT GTG GCA GAT GCT      2057
Leu His Thr Ala Val Pro Gly Pro Trp Gln Glu Asp Val Ala Asp Ala
        40                  45                  50

GAG GAG TGT GCT AGG CGC TGT GGG CCC CTT CTG GAC TGT CG GTGAGTGGCT    2108
Glu Glu Cys Ala Arg Arg Cys Gly Pro Leu Leu Asp Cys Ar
    55                  60                  65

AAGTAGCCTA GATATGGCTG AGGGCATGAG AATCTGGGTT GCCAGTTAAC TTTGTGTCTG   2168

CCACCCCCCC CCCCTTCTCC AG G GCC TTC CAC TAC AAC ATG AGC AGC CAT       2218
                        g Ala Phe His Tyr Asn Met Ser Ser His
                           70                  75

GGT TGC CAG CTG CTG CCG TGG ACC CAG CAC TCG CTG CAC ACA CAG CTA      2266
Gly Cys Gln Leu Leu Pro Trp Thr Gln His Ser Leu His Thr Gln Leu
                80                  85                  90

TAC CAC TCG AGT CTG TGC CAT CTC TTC CAG AAG AAA G GCAAGTGGTG        2313
Tyr His Ser Ser Leu Cys His Leu Phe Gln Lys Lys A
            95                  100

GTGAGGAGGG GAAACAGGCT GAGTAACAGG GGCCACGAGG CTCAGGCCTG TTGACCTTCC   2373

TCCATTGCTT CCAG AT TAT GTG CGG ACC TGC ATT ATG GAC AAT GGG GTC       2422
                  sp Tyr Val Arg Thr Cys Ile Met Asp Asn Gly Val
                              110                 115

AGC TAC CGG GGC ACT GTG GCC AGG ACA GCT GGT GGC CTG CCC TGC CAA      2470
Ser Tyr Arg Gly Thr Val Ala Arg Thr Ala Gly Gly Leu Pro Cys Gln
            120                 125                 130

GCC TGG AGT CGC AGG TTC CCC AAT GAC CAC AA GTGAGTCAGA CACTTCAGGT    2522
Ala Trp Ser Arg Arg Phe Pro Asn Asp His Ly
        135                 140

CAGACCGTTA GGCCTGAAGC AGTATTCCCC CAGTGTGCAC TGTAGTAAGA ATCTTTGTCT   2582

ACAG G TAT ACG CCC ACG CCA AAG AAT GGC CTG GAA GAG AAC TTC TGT       2629
      s Tyr Thr Pro Thr Pro Lys Asn Gly Leu Glu Glu Asn Phe Cys
            145                 150                 155

AGG AAC CCT GAT GGG GAT CCC AGA GGT CCC TGG TGC TAC ACA ACA AAC      2677
Arg Asn Pro Asp Gly Asp Pro Arg Gly Pro Trp Cys Tyr Thr Thr Asn
        160                 165                 170

CGC AGT GTG CGT TTC CAG AGC TGT GGC ATC AAA ACC TGC AGG GAG G       2723
Arg Ser Val Arg Phe Gln Ser Cys Gly Ile Lys Thr Cys Arg Glu A
    175                 180                 185

GTAAGCGGCT GGGGTCAATC AAGCCTAAGG AGGGAGTGAT AGGCCTGCCC CCACTTAGAA   2783
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GTGCATTGGC CCTGTTTCCA G CT GTT TGT GTT CTG TGC AAC GGT GAG GAT          2833
                        la Val Cys Val Leu Cys Asn Gly Glu Asp
                           190                 195

TAC CGT GGC GAG GTA GAC GTT ACA GAG TCA GGG CGG GAG TGT CAA CGC          2881
Tyr Arg Gly Glu Val Asp Val Thr Glu Ser Gly Arg Glu Cys Gln Arg
    200                 205                 210

TGG GAC CTG CAG CAC CCC CAC TCG CAC CCT TTC CAG CCT GAA AA               2925
Trp Asp Leu Gln His Pro His Ser His Pro Phe Gln Pro Glu Ly
215                 220                 225

GTATGTAGGC AGAATCCTTA TTTTGAGGGT GGGGCTCAGC TCTACTGGGA CTGAGTCCCA       2985

GAGTCTTGTT ACTGCTTTCA G G TTC CTA GAC AAA GAT CTG AAA GAC AAC TAT        3037
                       s Phe Leu Asp Lys Asp Leu Lys Asp Asn Tyr
                          230                 235

TGT CGT AAT CCG GAC GGA TCT GAG CGG CCC TGG TGC TAC ACC ACA GAC         3085
Cys Arg Asn Pro Asp Gly Ser Glu Arg Pro Trp Cys Tyr Thr Thr Asp
240                 245                 250                 255

CCG AAT GTT GAG CGA GAA TTC TGC GAC CTG CCC AGT TGC G GTAGGCTGCA        3135
Pro Asn Val Glu Arg Glu Phe Cys Asp Leu Pro Ser Cys G
                    260                 265

GGGTCAGGGT CTAGGAAGGA GCTTGGAAAA AACTGGCGGG CACGGTTCAA CTGGGAGAGG       3195

TACTAGGGAA GTTAGGCGTG GGTAGAGAGC AAAGCCTGCT GAGTACCAGA GACCAATTCC       3255

AGTTTTCGGT CAG GG CCT AAC CTG CCT CCG ACC GTC AAA GGA TCC AAG TCA        3306
                 ly Pro Asn Leu Pro Pro Thr Val Lys Gly Ser Lys Ser
                    270                 275                 280

CAG CGG CGC AAC AAG GGC AAG GCT CTT AAC TGC TTC CGC GGA AAA GGT         3354
Gln Arg Arg Asn Lys Gly Lys Ala Leu Asn Cys Phe Arg Gly Lys Gly
           285                 290                 295

GAA GAC TAT CGA GGC ACA ACC AAT ACC ACC TCT GCG GGC GTG CCC TGC         3402
Glu Asp Tyr Arg Gly Thr Thr Asn Thr Thr Ser Ala Gly Val Pro Cys
        300                 305                 310

CAG CGG TGG GAT GCG CAG AGT CCA CAC CAG CAC CGC TTT GTG CCA GAG         3450
Gln Arg Trp Asp Ala Gln Ser Pro His Gln His Arg Phe Val Pro Glu
     315                 320                 325

AAA TAT GCT TGC AA GTGAGGTGAC AGGCCGGAGC AGGGAGAGTG CACCTGTGGG          3504
Lys Tyr Ala Cys Ly
330

TGGAGGCAGA GCGTATGCGA AGGTGGGACC TGGGGGCGGA GTCAGAGGTT CCAGCCTACT       3564

GCGGGTTGGC TGGTGGGCTA GGTGGGACCC CACTCTCGAT AAGGGAAGTG ACTACTCAG       3623

G GAC CTT CGT GAG AAT TTC TGC CGG AAT CCT GAT GGC TCC GAG GCG            3669
s Asp Leu Arg Glu Asn Phe Cys Arg Asn Pro Asp Gly Ser Glu Ala
  335                 340                 345

CCT TGG TGC TTC ACA TCT CGA CCT GGT TTG CGC ATG GCC TTC TGC CAC         3717
Pro Trp Cys Phe Thr Ser Arg Pro Gly Leu Arg Met Ala Phe Cys His
350                 355                 360                 365

CAG ATC CCA CGC TGC ACT GAA GAA CTG GTG CCA GAG G GTGAGGCTGG            3764
Gln Ile Pro Arg Cys Thr Glu Glu Leu Val Pro Glu G
                    370                 375

AGCGGGGGTA CAGAATCTGG GCAGGAATCA ACCCAGGGCT GACCACCGCT CTTGCCTGCC       3824

CACCACAG GA TGC TAC CAC GGC TCA GGT GAA CAG TAT CGT GGC TCA GTC          3873
          ly Cys Tyr His Gly Ser Gly Glu Gln Tyr Arg Gly Ser Val
             380                 385                 390

AGC AAG ACG CGC AAG GGC GTT CAG TGC CAG CAC TGG TCC TCT GAG ACA         3921
Ser Lys Thr Arg Lys Gly Val Gln Cys Gln His Trp Ser Ser Glu Thr
           395                 400                 405

CCG CAC AAG CCA CA GTGAGTGTGT GCTATGTGCA GATAGGGCCT TAACTCTAGG          3975
Pro His Lys Pro Gl
        410
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GCAGAATACC TTAAGTTCTT GTGAGCCTAA AGAGGGTCTA AGTGGCCTGA TGTGTCCCCC      4035

TACCTCCTGC CCCTACATCT AG A TTT ACA CCC ACC TCG GCA CCG CAG GCG          4085
                          n Phe Thr Pro Thr Ser Ala Pro Gln Ala
                             415                 420

GGA CTG GAG GCC AAC TTC TGC AGG AAT CCT GAT GGG GAT AGC CAT GGG         4133
Gly Leu Glu Ala Asn Phe Cys Arg Asn Pro Asp Gly Asp Ser His Gly
          425                 430                 435

CCC TGG TGC TAT ACC TTG GAC CCG GAT ATC CTG TTT GAC TAC TGT GCC         4181
Pro Trp Cys Tyr Thr Leu Asp Pro Asp Ile Leu Phe Asp Tyr Cys Ala
     440                 445                 450

CTA CAG CGC TGT G GTTAGTGCTT AAGACTTCCC CTTGTCTGGG TTTCAAACCT          4234
Leu Gln Arg Cys A
     455

CACCTCCATA GACTGGCTCC CTTAACCTGA GTGAACTTGA TCTTGCAG AT GAT GAC        4290
                                                  sp Asp Asp
                                                     460

CAG CCA CCA TCC ATT CTG GAC CCC CCA G GTATGGGGTT GGGCCAATTG            4338
Gln Pro Pro Ser Ile Leu Asp Pro Pro A
               465

TGGGTACACA GTCTTTGACC CTGACCCTCA CTGAAGGTTT CATCCTGCCC CATCCCCAG      4397

AC CAG GTG GTG TTT GAA AAG TGT GGC AAG AGA GTT GAC AAG AGT AAT         4444
sp Gln Val Val Phe Glu Lys Cys Gly Lys Arg Val Asp Lys Ser Asn
               475                 480                 485

AAA CTT CGT GTG GTG GGA GGC CAT CCT GGG AAC TCC CCA TGG ACG GTC        4492
Lys Leu Arg Val Val Gly Gly His Pro Gly Asn Ser Pro Trp Thr Val
               490                 495                 500

AGC TTG CGG AAT CG GTGAGGCCTA AGCGCTTATC TCAAGGAGTG GAGGCTGGAA        4546
Ser Leu Arg Asn Ar
          505

ACTCTGTGGC TTTATCAGTA GAAGATGGAT GCCTGGCCTT GTACCAAAAG GTCCTTGTCA     4606

GAAATGACAG TCTAGCATGT GTCCCAGGAC TCAGTGTGGC TTCTCATCTT TACTCCTCTA     4666

G A CAG GGC CAG CAT TTC TGT GGG GGC TCC CTA GTG AAG GAG CAG TGG        4713
g Gln Gly Gln His Phe Cys Gly Gly Ser Leu Val Lys Glu Gln Trp
          510                 515                 520

GTA CTG ACT GCC CGG CAA TGC ATC TGG TCA TG GTGAGCAGAC TGGGGACTCC      4765
Val Leu Thr Ala Arg Gln Cys Ile Trp Ser Cy
          525                 530

TAGCCTACCT CTCCCTGCCA TTGTCTGTCC CACAAGCAAA CTAAATTGTG ACAGCTGATT     4825

GGGAGTCAAG CATGAACTAG CAGAGTCTCT TTCTCCCAG C CAC GAA CCT CTC ACA      4880
                                           s His Glu Pro Leu Thr
                                              535

GGA TAC GAG GTA TGG TTG GGT ACA ATT AAC CAG AAC CCA CAG CCT GGA        4928
Gly Tyr Glu Val Trp Leu Gly Thr Ile Asn Gln Asn Pro Gln Pro Gly
     540                 545                 550

GAG GCA AAC CTG CAG AGG GTC CCA GTG GCC AAG GCA GTG TGC GGC CCT        4976
Glu Ala Asn Leu Gln Arg Val Pro Val Ala Lys Ala Val Cys Gly Pro
     555                 560                 565

GCA GGC TCC CAG CTT GTT CTG CTC AAG CTG GAG AG GTATGTGGAT              5021
Ala Gly Ser Gln Leu Val Leu Leu Lys Leu Glu Ar
570                 575                 580

GTGTTGAGAG GGTGTGAGGC AGGGCTAGCC TCATGGTCAT AGGTCCTGAA AACCCTCATT     5081

CCCACTAAAG A CCT GTG ATC CTG AAC CAT CAC GTG GCC CTG ATT TGC CTG       5131
             g Pro Val Ile Leu Asn His His Val Ala Leu Ile Cys Leu
                585                 590

CCT CCT GAA CAG TAT GTG GTA CCT CCA GGG ACC AAG TGT GAG ATC GCA        5179
Pro Pro Glu Gln Tyr Val Val Pro Pro Gly Thr Lys Cys Glu Ile Ala
          595                 600                 605
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GGC TGG GGT GAA TCC ATC G GTAAGAGCAC AGTGCATAGA CATGGACTGC              5228
Gly Trp Gly Glu Ser Ile G
                615

TATGGGCCGG GAGGTCCAGC ACTGGTTTTG GCTCAAGGGT CCCCTCCTTA TCATTGTCTG      5288

TACTTCAG GT ACA AGC AAT AAC ACA GTC CTT CAT GTG GCC TCG ATG AAT         5337
          ly Thr Ser Asn Asn Thr Val Leu His Val Ala Ser Met Asn
                620                 625                 630

GTC ATC TCC AAC CAG GAA TGT AAC ACG AAG TAC CGA GGA CAC ATA CAA         5385
Val Ile Ser Asn Gln Glu Cys Asn Thr Lys Tyr Arg Gly His Ile Gln
            635                 640                 645

GAG AGT GAG ATA TGC ACC CAG GGA CTG GTG GTC CCT GTG GGG GCT TGT         5433
Glu Ser Glu Ile Cys Thr Gln Gly Leu Val Val Pro Val Gly Ala Cys
            650                 655                 660

GAG GTCAGTGGGA GAGCCCCTGG GCCAGCCTGG GAAGGGCTTG GGAGCTGAAA              5486
Glu

TTATAGTACT TGATTGCCAA GGGGGTGGGA TGTCAGGAGA GGGTAGTCAC TGCCGAGGTC      5546

CAGAGCCTTC ACCCGTTTTT CTACCTGCCA G GGT GAC TAC GGG GGC CCA CTT          5598
                                  Gly Asp Tyr Gly Gly Pro Leu
                                      665                 670

GCC TGC TAT ACC CAT GAC TGC TGG GTC CTA CAG GGA CTT ATC ATC CCG         5646
Ala Cys Tyr Thr His Asp Cys Trp Val Leu Gln Gly Leu Ile Ile Pro
            675                 680                 685

AAC AGA GTG TGT GCA CGG CCC CGC TGG CCA GCT ATC TTC ACA CGG GTG         5694
Asn Arg Val Cys Ala Arg Pro Arg Trp Pro Ala Ile Phe Thr Arg Val
            690                 695                 700

TCT GTG TTC GTG GAC TGG ATT AAC AAG GTC ATG CAG CTG GAG                 5736
Ser Val Phe Val Asp Trp Ile Asn Lys Val Met Gln Leu Glu
    705                 710                 715

TAGGCCTGCT TTTGAGCCCT TAGAGATGTC AAGACTTCTC AAACATAAAG CGGCCTTTTC      5796

TCTCTGTCTG TATAGAGTGC TTCTTAGTTTCTGT CTCTAGGGAA GGTGTTGACT CCTTGC      5856

AAGAGGCTGT GTGGCTTAAG ACCAGCACAC TCTAGGCTAA GTGCTCTGAT CCCAGAACAA      5916

CTTCAAAAGG TATGTACTGT GTGTGGGCAG GGTGCACCAT CTTCCAGAGG CACTCCTGGG      5976

AATGCAAGGA CAGTGCAGAA GTTCCCAGCC CATGGACCAG AGCAGAAAGA GTGATGTAGG      6036

TCTACACCAG TCCCGTTTGG CTAGGACAGG CAGGGGTTGA GTCTCTCATG GCTTCTCTCT      6096

GTCACATGAC AGGGATGAAT ACACTGTGGA TATCAAACCA AGGACCTAGG GTTTCTGAAC      6156

CCCAAGGTAG AGGCTGGGGC TGGGGATGGC TTGTACAAAG TACCAGCACA GACCAGGCTC      6216

TGTGTCCTCC TTTATTATGA TTAGAGTCCA TAGTCCTCTG CCCACTCATT CGGAGTCCAG      6276

AGCCCAGGAA ACCTCTAGGC AGTTCTGCCA GATCCTGGGG CTTACCGAAG AGCAAAGTTC      6336

GAGACGGACT GCCCAGCTCA CAAAGAGCAA CAGGGCTTCA GCTGCCCAAG TGTGTGTGTA      6396

GCCAAAGCAC AGTGTTCATG AAGCTGTCTG ATTCCACCTC CACCTCTGAC AGCGCATGGG      6456

TGCTCTTGGG ATACAGCAGG AGCCTGTATG AGCAGCAACA CATGACATTG GAGGGTCCTG      6516

TCCTGTTTAC CTGCCACCAG CTGCCCAACT ATCCTGTACA CTCACCGGAC AGGCACATTC      6576

CGGGCCTTGA GGGCATGGTA ATACTCCAGA CCCTGCTTGA AGGGTACACG CCGGTCCTCC      6636

TGGCCCAGCA TCAGTAACAC TGGTGTCTTT ACCTAGGTGT ATGGGAGGCA AGGAGCTGTG      6696

GCGAGCTGAG CTCTGGACTC TGGAGGAATG GGTGGCACAA GGATACCTGG GTACC            6751
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(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6100 base pairs
(B) TYPE: nucleic acid

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(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: genomic DNA

(i v) ANTI-SENSE: no

(v i) ORIGINAL SOURCE:
(A) ORGANISM: human
(D) DEVELOPMENTAL STAGE: fetal
(F) TISSUE TYPE: liver

(v i i) IMMEDIATE SOURCE:
(A) LIBRARY: genomic
(B) CLONE: L5/3

(v i i i) POSITION IN GENOME:
(A) CHROMOSOME/SEGMENT: human 3p21/D3F15S2

(i x) FEATURE:
(C) IDENTIFICATION METHOD: experimental
(D) OTHER INFORMATION: This is the combined sequence of the entire gene from two different recombinant phage isolates (L 5 & L 5 / 3).

(x) PUBLICATION INFORMATION:
(K) RELEVANT RESIDUES IN SEQ ID NO:6: FROM 1 TO 6100

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:6:

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CTGCAGAGGG GTTTCACCCC AACCCCAGGG CACCTCAAGT GTCCCCACCA AACCTTCCTA      60

ACACCTGTCC ACTAAGCTGT ACTAGGCCCT TGCAACTGAC CTATGGGACC CTGAGGCCTG     120

GCCCCTCATG GCTCCTGTCA CCAGGTCTCA GGTCAGGGTC CAGCAGGGCC CTGAGCTGAC     180

GTGTGGAGCC AGAGCCACCC AATCCCGTAG ACAGGTTTCA CAACTTCCCG GATGGGGCTG     240

TGGTGGGTCA CAGTGCAGCC TCCAGCCAGA AGG ATG GGG TGG CTC CCA CTC CTG       294
                                    Met Gly Trp Leu Pro Leu Leu
                                                5

CTG CTT CTG ACT CAA TGC TTA GGG GTC CCT G GTAAGTGCCC CCAACCCTGA        345
Leu Leu Leu Thr Gln Cys Leu Gly Val Pro G
        10                  15

TCCCCATCTG CCTTCAGGAG GGGGTTGGCC CCATTCTCCT ATTCTAGGAT GAGAAAAAAG     405

TCGGGAGCAG AGGCTCAGTG GGCATGGGGC AGTGACCTTG CCCTCTTGAG CACAGCTGGG     465

AAGCCCTAGG AACACATAGA CATTGCCCAC TTAGGCCTCT ATTAGCACGT CTGCTCTAGC     525

ACTGAAGCAG TGTCAGGACC ACACAGATGC ACGCACACAG CAGGCAGTGA CCCCTCCTGA     585

GCCTGATCTA CCCCTCTAAC CTAGCATATG CCTTTGTGCA GGTGAGAGCC CAGATTTGGA     645

GTCTGAATGC CTAGCCAGGG CCCTTGGCTG GGTAATGTGA TGGCTCTGAG CCTTAGCATT     705

CTCATTTGAG AGATGAGGTG GGGCAAGCTT CATCACCCAC TGCTCTCACA GAGCGTATGT     765

GTTAGATCTG AGCCCGGTGC CTGGGCCACT AAACAGAGGC ACCGGTGATA ACTACCAAGT     825

CTGGGCCTGC TTCCCAGGGG AAATTTTTTT CACAAGTATC TGTGCAGGGG GCTAGACTGG     885

CCCTTGAAAG TGCATACAGG GTCCATCCCA GAAGCTTGTA GCTTTGATCC CCTGAATGAA     945

CAAAGTGTGG ACATGCCAAT ACACATTACT GACATGTATG CCCACCTGAC CTGCACCCAC    1005

TCATGCCTAC TCTGCAG GG CAG CGC TCG CCA TTG AAT GAC TTC CAA GTG CTC    1057
                   ly Gln Arg Ser Pro Leu Asn Asp Phe Gln Val Leu
                             20                  25

CGG GGC ACA GAG CTA CAG CAC CTG CTA CAT GCG GTG GTG CCC GGG CCT      1105
Arg Gly Thr Glu Leu Gln His Leu Leu His Ala Val Val Pro Gly Pro
 30                  35                  40                  45

TGG CAG GAG GAT GTG GCA GAT GCT GAA GAG TGT GCT GGT CGC TGT GGG      1153
Trp Gln Glu Asp Val Ala Asp Ala Glu Glu Cys Ala Gly Arg Cys Gly
                    50                  55                  60
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CCC TTA ATG GAC TGC CG GTGAGTGGCC ACTGGGCTAG ATAAGACTGG                  1200
Pro Leu Met Asp Cys Ar
                  65

GGGCAGGGAA GCCTGGGCTG TGGCGTTACC CTGTGCCTTC TTCTCTCCAG G GCC TTC        1257
                                                         g Ala Phe

CAC TAC AAC GTG AGC AGC CAT GGT TGC CAA CTG CTG CCA TGG ACT CAA         1305
His Tyr Asn Val Ser Ser His Gly Cys Gln Leu Leu Pro Trp Thr Gln
 70                  75                  80                  85

CAC TCG CCC CAC ACG AGG CTG CGG CGT TCT GGG CGC TGT GAC CTC TTC         1353
His Ser Pro His Thr Arg Leu Arg Arg Ser Gly Arg Cys Asp Leu Phe
            90                  95                 100

CAG AAG AAA G GCAAGTGGGG GTGGAGAGGG GCAGGGTGGG AGACAGGGGA               1403
Gln Lys Lys A

CCTCAGCCCA AGTTGATCTT CTGTCTCTTG CTCCCAG AC TAC GTA CGG ACC TGC         1457
                                        sp Tyr Val Arg Thr Cys
                                                           110

ATC ATG AAC AAT GGG GTT GGG TAC CGG GGC ACC ATG GCC ACG ACC GTG         1505
Ile Met Asn Asn Gly Val Gly Tyr Arg Gly Thr Met Ala Thr Thr Val
                115                 120                 125

GGT GGC CTG CCC TGC CAG GCT TGG AGC CAC AAG TTC CCG AAT GAT CAC         1553
Gly Gly Leu Pro Cys Gln Ala Trp Ser His Lys Phe Pro Asn Asp His
            130                 135                 140

AA GTGAGACAAA CACCTTCCCT CCGTCCCGGC CTGGGGCTTC CCCCAGCACA               1605
Ly

CACTATAGTG ATGCTCTGGG CCCTCAG G TAC ACG CCC ACT CTC CGG AAT GGC         1657
                               s Tyr Thr Pro Thr Leu Arg Asn Gly
                                 145                 150

CTG GAA GAG AAC TTC TGC CGT AAC CCT GAT GGC GAC CCC GGA GGT CCT         1705
Leu Glu Glu Asn Phe Cys Arg Asn Pro Asp Gly Asp Pro Gly Gly Pro
            155                 160                 165

TGG TGC TAC ACA ACA GAC CCT GCT GTG CGC TTC CAG AGC TGC GGC ATC         1753
Trp Cys Tyr Thr Thr Asp Pro Ala Val Arg Phe Gln Ser Cys Gly Ile
        170                 175                 180

AAA TCC TGC CGG GAG G GTAAGCGGCG CCGGGTCAAG CTGGGAGAGT GGAGACAAGC       1809
Lys Ser Cys Arg Glu A
    185

CCACGTCCAT CCACGAACCC ACTGGCTCTT TGTCTCCAG CC GCG TGT GTC TGG TGC       1865
                                           la Ala Cys Val Trp Cys
                                             190

AAT GGC GAG GAA TAC CGC GGC GCG GTA GAC CGC ACG GAG TCA GGG CGC         1913
Asn Gly Glu Glu Tyr Arg Gly Ala Val Asp Arg Thr Glu Ser Gly Arg
195                 200                 205                 210

GAG TGC CAG CGC TGG GAT CTT CAG CAC CCG CAC CAG CAC CCC TTC GAG         1961
Glu Cys Gln Arg Trp Asp Leu Gln His Pro His Gln His Pro Phe Glu
                215                 220                 225

CCG GGC AA GTACGCGTAG GCGGTATCGG CGTCCTGGGG GCCGGGCTAG GGAAGGTCCA       2019
Pro Gly Ly

GGACTCCAGG GGCAGGGCTC CGTGTAGGGC AATTGGGCGG GGCCAGATAA GCCAGAGTCC       2079

CAGGGTCTTG TTCACGCCCC ATTACCGCCC CCAG G TTC CTC GAC CAA GGT CTG         2132
                                      s Phe Leu Asp Gln Gly Leu
                                        230                 235

GAC GAC AAC TAT TGC CGG AAT CCT GAC GGC TCC GAG CGG CCA TGG TGC         2180
Asp Asp Asn Tyr Cys Arg Asn Pro Asp Gly Ser Glu Arg Pro Trp Cys
            240                 245                 250

TAC ACT ACG GAT CCG CAG ATC GAG CGA GAG TTC TGT GAC CTC CCC CGC         2228
Tyr Thr Thr Asp Pro Gln Ile Glu Arg Glu Phe Cys Asp Leu Pro Arg
        255                 260                 265

TGC G GTAGGCGGCG GGGACCAGGC CTGGGAGGGT ACCTGGGAAC CTTGGGGAGG           2282
Cys G
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GGCGTGGCTT GGCCGGGGAG GTAAGAGGGG CTGGGCGTGA CCTGAGAGCA TACCCCGTGG    2342

AGTACCGTAC ACCTGGGAAA GGCGGGTTTG GTCCCAGCCC CAGAGGGATC TCAGCTCTCG    2402

CTCGGGGCCC GACCTATCTC GGTCCATCTA AG GG TCC GAG GCA CAG CCC CGC       2454
                                     ly Ser Glu Ala Gln Pro Arg
                                        270                 275

CAA GAG GCC ACA ACT GTC AGC TGC TTC CGC GGG AAG GGT GAG GGC TAC      2502
Gln Glu Ala Thr Thr Val Ser Cys Phe Arg Gly Lys Gly Glu Gly Tyr
                 280                 285                 290

CGG GGC ACA GCC AAT ACC ACC ACT GCG GGC GTA CCT TGC CAG CGT TGG      2550
Arg Gly Thr Ala Asn Thr Thr Thr Ala Gly Val Pro Cys Gln Arg Trp
            295                 300                 305

GAC GCG CAA ATC CCT CAT CAG CAC CGA TTT ACG CCA GAA AAA TAC GCG      2598
Asp Ala Gln Ile Pro His Gln His Arg Phe Thr Pro Glu Lys Tyr Ala
        310                 315                 320

TGC AA GTGAGGTGGG GGGGGGGGGC GGGCGTTGGG ACGTGCTGCT GCGGGTGAGA       2653
Cys Ly

CGGGAGGAAG GTAGTCACGG GCTCAAGGCT GGAGGCTGGC GGGCTAGGGC TGAGTGGAGC    2713

GCCTGCTTAG A GAC CTT CGG GAG AAC TTC TGC CGG AAC CCC GAC GGC TCA      2763
            s Asp Leu Arg Glu Asn Phe Cys Arg Asn Pro Asp Gly Ser
                                330                 335

GAG GCG CCC TGG TGC TTC ACA CTG CGG CCC GGC ATG CGC GCG GCC TTT      2811
Glu Ala Pro Trp Cys Phe Thr Leu Arg Pro Gly Met Arg Ala Ala Phe
    340                 345                 350

TGC TAC CAG ATC CGG CGT TGT ACA GAC GAC GTG CGG CCC CAG G            2854
Cys Tyr Gln Ile Arg Arg Cys Thr Asp Asp Val Arg Pro Gln A
355                 360                 365

GTGAGGCCCA AGCTTGGGGG CTACAGAGCC GGGCTGGAAG CTGGAACCGG AGGCCGGGGC    2914

GAGGTCTCGG CCTGATGGCT GCCCGCACCC GCCACAG   AC TGC TAC CAC GGC GCA     2968
                                          sp Cys Tyr His Gly Ala
                                             370

GGG GAG CAG TAC CGC GGC ACG GTC AGC AAG ACC CGC AAG GGT GTC CAG      3016
Gly Glu Gln Tyr Arg Gly Thr Val Ser Lys Thr Arg Lys Gly Val Gln
                    375                 380                 385

TGC CAG CGC TGG TCC GCT GAG ACG CCG CAC AAG CCG CA GTGAGTCCCT        3064
Cys Gln Arg Trp Ser Ala Glu Thr Pro His Lys Pro Gl
                395                 400

GGTGCTCCCG GCCCCGCCAG GGCCCTAACC CTGGGGCGGC ATGCTTTGGT GTCTGGGACC    3124

AGAGCCTGGA AATGGTTGAG ACTACCCTGC CACGATTTTG CTCCCGCTTC CGCCTAG G     3182
                                                                  n

TTC ACG TTT ACC TCC GAA CCG CAT GCA CAA CTG GAG GAG AAC TTC TGC       3230
Phe Thr Phe Thr Ser Glu Pro His Ala Gln Leu Glu Glu Asn Phe Cys
    405                 410                 415

CGG AAC CCA GAT GGG GAT AGC CAT GGG CCC TGG TGC TAC ACG ATG GAC      3278
Arg Asn Pro Asp Gly Asp Ser His Gly Pro Trp Cys Tyr Thr Met Asp
420                 425                 430                 435

CCA AGG ACC CCA TTC GAC TAC TGT GCC CTG CGA CGC TGC G GTGAGCACTA     3328
Pro Arg Thr Pro Phe Asp Tyr Cys Ala Leu Arg Arg Cys A
                440                 445

GTGACGCTTC CCCCATGACC CTGCCTCAGC CCCCACCCAA AGGCTGGCTC CCTTAACCCC    3388

AGTGAACTTT GTCTTTCAG CT GAT GAC CAG CCG CCA TCA ATC CTG GAC CCC       3439
                      la Asp Asp Gln Pro Pro Ser Ile Leu Asp Pro
                         450                 455

CCA G GTTAGGAGTT GGGCCAGTTA TGGGTCAGGC CCTTTAGCCC ACGACATCCA         3493
Pro A

CACAGTCTGG GTTTCATCCA GCCCACCCCA TCCTACAG AC CAG GTG CAG TTT GAG     3548
                                          sp Gln Val Gln Phe Glu
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                                                                  465

AAG TGT GGC AAG AGG GTG GAT CGG CTG GAT CAG CGG CGT TCC AAG CTG      3596
Lys Cys Gly Lys Arg Val Asp Arg Leu Asp Gln Arg Arg Ser Lys Leu
            470                 475                 480

CGC GTG GTT GGG GGC CAT CCG GGC AAC TCA CCC TGG ACA GTC AGC TTG      3644
Arg Val Val Gly Gly His Pro Gly Asn Ser Pro Trp Thr Val Ser Leu
        485                 490                 495

CGG AAT CG GTGAGGCACA ACTGCCTGTC TCCCACAGAG AGGAGCTGAG GTTGTGTCCT    3702
Arg Asn Ar
    500

CTGTGGTTAT CCACTGGGGC TGGGAATCTA TCCGTGCCCC TTGAGAGGTC CTAGCCAAGA    3762

AGATGGCAGG TCTTACGAAT CTGTCCCAGG AGTCTGTTAC CTGTCCTAAT TCCCCACTCC    3822

TCTAG G CAG GGC CAG CAT TTC TGC GGG GGG TCT CTA GTG AAG GAG CAG      3870
      g Gln Gly Gln His Phe Cys Gly Gly Ser Leu Val Lys Glu Gln
                505                 510                 515

TGG ATA CTG ACT GCC CGG CAG TGC TTC TCC TCC TG GTGAGCCTCC           3915
Trp Ile Leu Thr Ala Arg Gln Cys Phe Ser Ser Cy
            520                 525

CTTGTGTTTG GGGACCCAGT CTCATCCCAC CTTCCCCCTT CCCCAGGCAA GCTAACAAGT    3975

GAGCCTTGGG GCAATGGACT GAGAGTCACA AATGACCTAG CAGAGCTTCT CTCCCAG C     4033
                                                                 s

CAT ATG CCT CTC ACG GGC TAT GAG GTA TGG TTG GGC ACC CTG TTC CAG      4081
His Met Pro Leu Thr Gly Tyr Glu Val Trp Leu Gly Thr Leu Phe Gln
        530                 535                 540

AAC CCA CAG CAT GGA GAG CCA AGC CTA CAG CGG GTC CCA GTA GCC AAG      4129
Asn Pro Gln His Gly Glu Pro Ser Leu Gln Arg Val Pro Val Ala Lys
    545                 550                 555

ATG GTG TGT GGG CCC TCA GGC TCC CAG CTT GTC CTG CTC AAG CTG GAG      4177
Met Val Cys Gly Pro Ser Gly Ser Gln Leu Val Leu Leu Lys Leu Glu
560                 565                 570                 575

AG GTATGTGGAC AACCTGGGAG GGTGTGAGGT GGGGCTGGGC CTTGTGGCCT           4229
Ar

CAGACCCTGA GTGCCCCCAT TCTTGCTAAA G A TCT GTG ACC CTG AAC CAG CGT    4282
                                  g Ser Val Thr Leu Asn Gln Arg
                                                  580

GTG GCC CTG ATC TGC CTG CCC CCT GAA TGG TAT GTG GTG CCT CCA GGG      4330
Val Ala Leu Ile Cys Leu Pro Pro Glu Trp Tyr Val Val Pro Pro Gly
    585                 590                 595

ACC AAG TGT GAG ATT GCA GGC TGG GGT GAG ACC AAA G GTAAGAGCAC        4377
Thr Lys Cys Glu Ile Ala Gly Trp Gly Glu Thr Lys G
600                 605                 610

AGTGCACAGG ACTGCTGGTG GCCAGGAGGC CAGCCCTGGA TCTTCCTGCA GGACCCTCTC    4437

CCTCTCCCCA TTCCCCTCAC TGCAG GT ACG GGT AAT GAC ACA GTC CTA AAT       4488
                              ly Thr Gly Asn Asp Thr Val Leu Asn
                                          615                 620

GTG GCC TTG CTG AAT GTC ATC TCC AAC CAG GAG TGT AAC ATC AAG CAC      4536
Val Ala Leu Leu Asn Val Ile Ser Asn Gln Glu Cys Asn Ile Lys His
            625                 630                 635

CGA GGA CGT GTG CGG GAG AGT GAG ATG TGC ACT GAG GGA CTG TTG GCC      4584
Arg Gly Arg Val Arg Glu Ser Glu Met Cys Thr Glu Gly Leu Leu Ala
        640                 645                 650

CCT GTG GGG GCC TGT GAG GTTGGTGGCA GGGCCTGGGC AGCCCTGGAA            4632
Pro Val Gly Ala Cys Glu
        655

GTATGGGGGG CTAGAAATGA ACTATTTTAT CATGAAGCAG GCTAGTCATT GCTGTGGCCC    4692

GGGGCCTCAT CAGTTCTCCT ACCTGCCAG GGT GAC TAC GGG GGC CCA CTT GCC      4745
                                  Gly Asp Tyr Gly Gly Pro Leu Ala
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                                                660                 665

TGC TTT ACC CAC AAC TGC TGG GTC CTG GAA GGA ATT ATA ATC CCC AAC          4793
Cys Phe Thr His Asn Cys Trp Val Leu Glu Gly Ile Ile Ile Pro Asn
            670                 675                 680

CGA GTA TGC GCA AGG TCC CGC TGG CCA GCT GTC TTC ACG CGT GTC TCT          4841
Arg Val Cys Ala Arg Ser Arg Trp Pro Ala Val Phe Thr Arg Val Ser
        685                 690                 695

GTG TTT GTG GAC TGG ATT CAC AAG GTC ATG AGA CTG GGT TAGGCCCAGC           4890
Val Phe Val Asp Trp Ile His Lys Val Met Arg Leu Gly
    700                 705                 710

CTTGATGCCA TATGCCTTGG GGAGGACAAA ACTTCTTGTC AGACATAAAG CCATGTTTCC       4950

TCTTTATGCC TGTACAGATG CTTCTTAGCC TTTGCTTCCA GGAAATGTGT CAGTGACTCC       5010

TTGCTAGGGC TCGGGTGGCT TGAGCCCAGC ACACCCTGGG CTAGGTGATC TGTCCAGCCT       5070

AGGGGCTTCC CCAACCAAGG CAATGTCCCT GGGACTACTT TTGCCCATGG GTGCCGTGGA       5130

AAGACAGGGC CTCACACTAG TCCTCCAGAC ATACTCTTGG GAAGGGTGGT ACAGAGTAGT       5190

TGCTAATGGA AGGGGCTGCA GCAGGGAAGC TAGGCTGGTA CAGAGTCCTG GTTGCCAGGA       5250

CAGGCAGAGG CTAAGCCTCT CACTGTTCCC TCCCTTCTCA CACTGGAGGC AGATGAAGCC       5310

CTTGTGGCTG CCACACCCAG AACCTAGGGT CTCTGCACCC CAGAGTGGGA GGTGGGGTTG       5370

GGGATGGTTT GGTACAAAGT ACCAGCAGGA ACCAGGCTCT GTGTCCTAAT TTATTATGAC       5430

TACATAGCCC ACATTCCTCT GCCCATGCAT CCGTGGAGTC CAGAGCCCAG AAAGCCTCCT       5490

GCTGCCCTGC CAGACCGTTG AGCTCCTCAA GAGGAAGTGT GGCACAGGCT GATCAGCTCA       5550

TGCAGAATGG CAGGGCTTCA GCTGCCCAAG TGTGTGCGTA GCCAGAGCAC AGCATTCATG       5610

AAGCTGTCTG ACTCCACCTC CACCTCTGAT AATGCGTGGG TGCTTTTGGG ATAGAGCAGG       5670

AGCCTGTAGG GATTAGTCAG CAACATTTAA GGTTGGAGGG TCCTCCTGTG CTCACCTGCC       5730

CACCAGCTGC CAGGGCCTTC ATGCTGCACT CACCGAACAG GCACATTCCG GGTCTTGAGG       5790

GCACGGTAAT ACTCCATGCC CTGCTTGAAG GGCACACGCC GGTCCTCCTG GCCCAACATC       5850

AGTAACAGTG GTGTCTTCAC CTGGGTGTTT GGGGAAGAGT GGGGAGCTGT GTTGAGCTGG       5910

GCCCTGGATT CTGGATGGAT GGGCAGCACA CAGGGCAAGC AGGGGGCTGC ATACCTGAGG       5970

GATGTATCTG ATGGGCGATT TGTCCAGCAT CTCAGCCCAC ACGCTGAGGT CTGGCAGGCA       6030

GTCACTGCTG AAAGGAAAGC CAGCCTCCAC CACGCACCTG CAAGACACCG AGCTGTTGCA       6090

GCCCCAGGAA                                                              6100
```

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2262 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: cDNA to mRNA
(A) DESCRIPTION: Identical to sequence ID NO: 1: with 5' and 3'adaptors added to make a full-length cDNA

(i v) ANTI-SENSE: no

(v i) ORIGINAL SOURCE:
(A) ORGANISM: human
(D) DEVELOPMENTAL STAGE: fetal
(F) TISSUE TYPE: liver

(v i i) IMMEDIATE SOURCE:
(A) LIBRARY: cDNA
(B) CLONE: #33 including 5'and 3'adaptors

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(x) PUBLICATION INFORMATION:

(K) RELEVANT RESIDUES IN SEQ ID NO: 7: FROM 1 TO 2262

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:7:

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AATTCCACC ATG GGG TGG CTC CCA AAT TCC GTC CTG CTG CTT CTG ACT          48
          Met Gly Trp Leu Pro Asn Ser Val Leu Leu Leu Leu Thr
                          5                  10

CAA TAC TTA GGG GTC CCT GGG CAG CGC TCG CCA TTG AAT GAC TTC CAA         96
Gln Tyr Leu Gly Val Pro Gly Gln Arg Ser Pro Leu Asn Asp Phe Gln
    15                  20                  25

GTG CTC CGG GGC ACA GAG CTA CAG CAC CTG CTA CAT GCG GTG GTG CCC        144
Val Leu Arg Gly Thr Glu Leu Gln His Leu Leu His Ala Val Val Pro
30                  35                  40                  45

GGG CCT TGG CAG GAG GAT GTG GCA GAT GCT GAA GAG TGT GCT GGT CGC        192
Gly Pro Trp Gln Glu Asp Val Ala Asp Ala Glu Glu Cys Ala Gly Arg
                50                  55                  60

TGT GGG CCC TTA ATG GAC TGC CGG GCC TTC CAC TAC AAC GTG AGC AGC        240
Cys Gly Pro Leu Met Asp Cys Arg Ala Phe His Tyr Asn Val Ser Ser
            65                  70                  75

CAT GGT TGC CAA CTG CTG CCA TGG ACT CAA CAC TCG CCC CAC ACG AGG        288
His Gly Cys Gln Leu Leu Pro Trp Thr Gln His Ser Pro His Thr Arg
        80                  85                  90

CTG CGG CGT TCT GGG CGC TGT GAC CTC TTC CAG AAG AAA GAC TAC GTA        336
Leu Arg Arg Ser Gly Arg Cys Asp Leu Phe Gln Lys Lys Asp Tyr Val
    95                  100                 105

CGG ACC TGC ATC ATG AAC AAT GGG GTT GGG TAC CGG GGC ACC ATG GCC        384
Arg Thr Cys Ile Met Asn Asn Gly Val Gly Tyr Arg Gly Thr Met Ala
110                 115                 120                 125

ACG ACC GTG GGT GGC CTG CCC TGC CAG GCT TGG AGC CAC AAG TTC CCG        432
Thr Thr Val Gly Gly Leu Pro Cys Gln Ala Trp Ser His Lys Phe Pro
                130                 135                 140

AAT GAT CAC AAG TAC ACG CCC ACT CTC CGG AAT GGC CTG GAA GAG AAC        480
Asn Asp His Lys Tyr Thr Pro Thr Leu Arg Asn Gly Leu Glu Glu Asn
            145                 150                 155

TTC TGC CGT AAC CCT GAT GGC GAC CCC GGA GGT CCT TGG TGC TAC ACA        528
Phe Cys Arg Asn Pro Asp Gly Asp Pro Gly Gly Pro Trp Cys Tyr Thr
        160                 165                 170

ACA GAC CCT GCT GTG CGC TTC CAG AGC TGC GGC ATC AAA TCC TGC CGG        576
Thr Asp Pro Ala Val Arg Phe Gln Ser Cys Gly Ile Lys Ser Cys Arg
    175                 180                 185

GAG GCC GCG TGT GTC TGG TGC AAT GGC GAG GAA TAC CGC GGC GCG GTA        624
Glu Ala Ala Cys Val Trp Cys Asn Gly Glu Glu Tyr Arg Gly Ala Val
190                 195                 200                 205

GAC CGC ACG GAG TCA GGG CGC GAG TGC CAG CGC TGG GAT CTT CAG CAC        672
Asp Arg Thr Glu Ser Gly Arg Glu Cys Gln Arg Trp Asp Leu Gln His
                210                 215                 220

CCG CAC CAG CAC CCC TTC GAG CCG GGC AAG TTC CTC GAC CAA GGT CTG        720
Pro His Gln His Pro Phe Glu Pro Gly Lys Phe Leu Asp Gln Gly Leu
            225                 230                 235

GAC GAC AAC TAT TGC CGG AAT CCT GAC GGC TCC GAG CGG CCA TGG TGC        768
Asp Asp Asn Tyr Cys Arg Asn Pro Asp Gly Ser Glu Arg Pro Trp Cys
        240                 245                 250

TAC ACT ACG GAT CCG CAG ATC GAG CGA GAG TTC TGT GAC CTC CCC CGC        816
Tyr Thr Thr Asp Pro Gln Ile Glu Arg Glu Phe Cys Asp Leu Pro Arg
    255                 260                 265

TGC GGG TCC GAG GCA CAG CCC CGC CAA GAG GCC ACA ACT GTC AGC TGC        864
Cys Gly Ser Glu Ala Gln Pro Arg Gln Glu Ala Thr Thr Val Ser Cys
270                 275                 280                 285

TTC CGC GGG AAG GGT GAG GGC TAC CGG GGC ACA GCC AAT ACC ACC ACT        912
Phe Arg Gly Lys Gly Glu Gly Tyr Arg Gly Thr Ala Asn Thr Thr Thr
                290                 295                 300
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GCG GGC GTA CCT TGC CAG CGT TGG GAC GCG CAA ATC CCT CAT CAG CAC          960
Ala Gly Val Pro Cys Gln Arg Trp Asp Ala Gln Ile Pro His Gln His
            305                 310                 315

CGA TTT ACG CCA GAA AAA TAC GCG TGC AAA GAC CTT CGG GAG AAC TTC         1008
Arg Phe Thr Pro Glu Lys Tyr Ala Cys Lys Asp Leu Arg Glu Asn Phe
        320                 325                 330

TGC CGG AAC CCC GAC GGC TCA GAG GCG CCC TGG TGC TTC ACA CTG CGG         1056
Cys Arg Asn Pro Asp Gly Ser Glu Ala Pro Trp Cys Phe Thr Leu Arg
    335                 340                 345

CCC GGC ATG CGC GCG GCC TTT TGC TAC CAG ATC CGG CGT TGT ACA GAC         1104
Pro Gly Met Arg Ala Ala Phe Cys Tyr Gln Ile Arg Arg Cys Thr Asp
350                 355                 360                 365

GAC GTG CGG CCC CAG GAC TGC TAC CAC GGC GCA GGG GAG CAG TAC CGC         1152
Asp Val Arg Pro Gln Asp Cys Tyr His Gly Ala Gly Glu Gln Tyr Arg
                370                 375                 380

GGC ACG GTC AGC AAG ACC CGC AAG GGT GTC CAG TGC CAG CGC TGG TCC         1200
Gly Thr Val Ser Lys Thr Arg Lys Gly Val Gln Cys Gln Arg Trp Ser
            385                 390                 395

GCT GAG ACG CCG CAC AAG CCG CAG TTC ACG TTT ACC TCC GAA CCG CAT         1248
Ala Glu Thr Pro His Lys Pro Gln Phe Thr Phe Thr Ser Glu Pro His
        400                 405                 410

GCA CAA CTG GAG GAG AAC TTC TGC CGG AAC CCA GAT GGG GAT AGC CAT         1296
Ala Gln Leu Glu Glu Asn Phe Cys Arg Asn Pro Asp Gly Asp Ser His
    415                 420                 425

GGG CCC TGG TGC TAC ACG ATG GAC CCA AGG ACC CCA TTC GAC TAC TGT         1344
Gly Pro Trp Cys Tyr Thr Met Asp Pro Arg Thr Pro Phe Asp Tyr Cys
430                 435                 440                 445

GCC CTG CGA CGC TGC GCT GAT GAC CAG CCG CCA TCA ATC CTG GAC CCC         1392
Ala Leu Arg Arg Cys Ala Asp Asp Gln Pro Pro Ser Ile Leu Asp Pro
                450                 455                 460

CCA GAC CAG GTG CAG TTT GAG AAG TGT GGC AAG AGG GTG GAT CGG CTG         1440
Pro Asp Gln Val Gln Phe Glu Lys Cys Gly Lys Arg Val Asp Arg Leu
            465                 470                 475

GAT CAG CGG CGT TCC AAG CTG CGC GTG GTT GGG GGC CAT CCG GGC AAC         1488
Asp Gln Arg Arg Ser Lys Leu Arg Val Val Gly Gly His Pro Gly Asn
        480                 485                 490

TCA CCC TGG ACA GTC AGC TTG CGG AAT CGG CAG GGC CAG CAT TTC TGC         1536
Ser Pro Trp Thr Val Ser Leu Arg Asn Arg Gln Gly Gln His Phe Cys
    495                 500                 505

GGG GGG TCT CTA GTG AAG GAG CAG TGG ATA CTG CTC ACT GCC CGG CAG TGC     1584
Gly Gly Ser Leu Val Lys Glu Gln Trp Ile Leu Leu Thr Ala Arg Gln Cys
510                 515                 520                 525

TTC TCC TCC TGC CAT ATG CCT CTC ACG GGC TAT GAG GTA TGG TTG GGC         1632
Phe Ser Ser Cys His Met Pro Leu Thr Gly Tyr Glu Val Trp Leu Gly
                530                 535                 540

ACC CTG TTC CAG AAC CCA CAG CAT GGA GAG CCA AGC CTA CAG CGG GTC         1680
Thr Leu Phe Gln Asn Pro Gln His Gly Glu Pro Ser Leu Gln Arg Val
            545                 550                 555

CCA GTA GCC AAG ATG GTG TGT GGG CCC TCA GGC TCC CAG CTT GTC CTG         1728
Pro Val Ala Lys Met Val Cys Gly Pro Ser Gly Ser Gln Leu Val Leu
        560                 565                 570

CTC AAG CTG GAG AGA TCT GTG ACC CTG AAC CAG CGC GTG GCC CTG ATC         1776
Leu Lys Leu Glu Arg Ser Val Thr Leu Asn Gln Arg Val Ala Leu Ile
    575                 580                 585

TGC CTG CCC CCT GAA TGG TAT GTG GTG CCT CCA GGG ACC AAG TGT GAG         1824
Cys Leu Pro Pro Glu Trp Tyr Val Val Pro Pro Gly Thr Lys Cys Glu
590                 595                 600                 605

ATT GCA GGC TGG GGT GAG ACC AAA GGT ACG GGT AAT GAC ACA GTC CTA         1872
Ile Ala Gly Trp Gly Glu Thr Lys Gly Thr Gly Asn Asp Thr Val Leu
                610                 615                 620
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AAT GTG GCC TTG CTG AAT GTC ATC TCC AAC CAG GAG TGT AAC ATC AAG        1920
Asn Val Ala Leu Leu Asn Val Ile Ser Asn Gln Glu Cys Asn Ile Lys
                625                 630                 635

CAC CGA GGA CGT GTG CGT GAG AGT GAG ATG TGC ACT GAG GGA CTG TTG        1968
His Arg Gly Arg Val Arg Glu Ser Glu Met Cys Thr Glu Gly Leu Leu
            640                 645                 650

GCC CCT GTG GGG GCC TGT GAG GGT GAC TAC GGG GGC CCA CTT GCC TGC        2016
Ala Pro Val Gly Ala Cys Glu Gly Asp Tyr Gly Gly Pro Leu Ala Cys
        655                 660                 665

TTT ACC CAC AAC TGC TGG GTC CTG GAA GGA ATT ATA ATC CCC AAC CGA        2064
Phe Thr His Asn Cys Trp Val Leu Glu Gly Ile Ile Ile Pro Asn Arg
670                 675                 680                 685

GTA TGC GCA AGG TCC CGC TGG CCA GCT GTC TTC ACG CGT GTC TCT GTG        2112
Val Cys Ala Arg Ser Arg Trp Pro Ala Val Phe Thr Arg Val Ser Val
                690                 695                 700

TTT GTG GAC TGG ATT CAC AAG GTC ATG AGA CTG GGT TAGGCCCAGC             2158
Phe Val Asp Trp Ile His Lys Val Met Arg Leu Gly
            705                 710

CTTGATGCCA TATGCCTTGG GGAGGACAAA ACTTCTTGTC AGACATAAAG CCATGTTTCC      2218

TCTTTATGCC TGTAAAAAAA AAAAAAAAGA ACGCCCCATG GTGG                       2262
```

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 711 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: protein

(i x) FEATURE:
(A) NAME/KEY: signal sequence
(B) LOCATION: 1 to 31
(C) IDENTIFICATION METHOD: similarity to other signal sequences; hydrophobic; numbered 1 to 31 since we do not if the actual signal peptidase site is after amino acid 31 or not; this has not been determined experimentally. We do know that the protein is secreted.
(D) OTHER INFORMATION: This sequence has a polymorphism at amino acid 13; a Cys is shown here, the other amino acid is Tyr.

(x) PUBLICATION INFORMATION:
(A) AUTHORS: Han, Su, Stuart, Lorie A., Degen, Sandra J. Friezner
(B) TITLE: Characterization of the DNF15S2 locus on human chromosome 3: Identification of a gene coding for four kringle domains with homology to hepatocyte growth factor
(C) JOURNAL: Biochemistry
(D) VOLUME: 30
(E) ISSUE: 40
(F) PAGES: 9768-9780
(G) DATE: 8 October 1991
(K) RELEVANT RESIDUES IN SEQ ID NO: 8: FROM 1 TO 711

(x i) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

```
Met Gly Trp Leu Pro Leu Leu Leu Leu Leu Thr Gln Cys Leu Gly Val
                5                  10                  15

Pro Gly Gln Arg Ser Pro Leu Asn Asp Phe Gln Val Leu Arg Gly Thr
            20                  25                  30

Glu Leu Gln His Leu Leu His Ala Val Val Pro Gly Pro Trp Gln Glu
        35                  40                  45

Asp Val Ala Asp Ala Glu Glu Cys Ala Gly Arg Cys Gly Pro Leu Met
    50                  55                  60

Asp Cys Arg Ala Phe His Tyr Asn Val Ser Ser His Gly Cys Gln Leu
65                  70                  75                  80
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Leu Pro Trp Thr Gln His Ser Pro His Thr Arg Leu Arg Arg Ser Gly
85 90 95

Arg Cys Asp Leu Phe Gln Lys Lys Asp Tyr Val Arg Thr Cys Ile Met
100 105 110

Asn Asn Gly Val Gly Tyr Arg Gly Thr Met Ala Thr Thr Val Gly Gly
115 120 125

Leu Pro Cys Gln Ala Trp Ser His Lys Phe Pro Asn Asp His Lys Tyr
130 135 140

Thr Pro Thr Leu Arg Asn Gly Leu Glu Glu Asn Phe Cys Arg Asn Pro
145 150 155 160

Asp Gly Asp Pro Gly Gly Pro Trp Cys Tyr Thr Thr Asp Pro Ala Val
165 170 175

Arg Phe Gln Ser Cys Gly Ile Lys Ser Cys Arg Glu Ala Ala Cys Val
180 185 190

Trp Cys Asn Gly Glu Glu Tyr Arg Gly Ala Val Asp Arg Thr Glu Ser
195 200 205

Gly Arg Glu Cys Gln Arg Trp Asp Leu Gln His Pro His Gln His Pro
210 215 220

Phe Glu Pro Gly Lys Phe Leu Asp Gln Gly Leu Asp Asp Asn Tyr Cys
225 230 235 240

Arg Asn Pro Asp Gly Ser Glu Arg Pro Trp Cys Tyr Thr Thr Asp Pro
245 250 255

Gln Ile Glu Arg Glu Phe Cys Asp Leu Pro Arg Cys Gly Ser Glu Ala
260 265 270

Gln Pro Arg Gln Glu Ala Thr Thr Val Ser Cys Phe Arg Gly Lys Gly
275 280 285

Glu Gly Tyr Arg Gly Thr Ala Asn Thr Thr Thr Ala Gly Val Pro Cys
290 295 300

Gln Arg Trp Asp Ala Gln Ile Pro His Gln His Arg Phe Thr Pro Glu
305 310 315 320

Lys Tyr Ala Cys Lys Asp Leu Arg Glu Asn Phe Cys Arg Asn Pro Asp
325 330 335

Gly Ser Glu Ala Pro Trp Cys Phe Thr Leu Arg Pro Gly Met Arg Ala
340 345 350

Ala Phe Cys Tyr Gln Ile Arg Arg Cys Thr Asp Asp Val Arg Pro Gln
355 360 365

Asp Cys Tyr His Gly Ala Gly Glu Gln Tyr Arg Gly Thr Val Ser Lys
370 375 380

Thr Arg Lys Gly Val Gln Cys Gln Arg Trp Ser Ala Glu Thr Pro His
385 390 395 400

Lys Pro Gln Phe Thr Phe Thr Ser Glu Pro His Ala Gln Leu Glu Glu
405 410 415

Asn Phe Cys Arg Asn Pro Asp Gly Asp Ser His Gly Pro Trp Cys Tyr
420 425 430

Thr Met Asp Pro Arg Thr Pro Phe Asp Tyr Cys Ala Leu Arg Arg Cys
435 440 445

Ala Asp Asp Gln Pro Pro Ser Ile Leu Asp Pro Pro Asp Gln Val Gln
450 455 460

Phe Glu Lys Cys Gly Lys Arg Val Asp Arg Leu Asp Gln Arg Arg Ser
465 470 475 480

Lys Leu Arg Val Val Gly Gly His Pro Gly Asn Ser Pro Trp Thr Val
485 490 495

Ser Leu Arg Asn Arg Gln Gly Gln His Phe Cys Gly Gly Ser Leu Val

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                        500                                         505                                         510

Lys Glu Gln Trp Ile Leu Thr Ala Arg Gln Cys Phe Ser Ser Cys His
        515                 520                 525

Met Pro Leu Thr Gly Tyr Glu Val Trp Leu Gly Thr Leu Phe Gln Asn
    530                 535                 540

Pro Gln His Gly Glu Pro Ser Leu Gln Arg Val Pro Val Ala Lys Met
545                 550                 555                 560

Val Cys Gly Pro Ser Gly Ser Gln Leu Val Leu Leu Lys Leu Glu Arg
                565                 570                 575

Ser Val Thr Leu Asn Gln Arg Val Ala Leu Ile Cys Leu Pro Pro Glu
            580                 585                 590

Trp Tyr Val Val Pro Pro Gly Thr Lys Cys Glu Ile Ala Gly Trp Gly
        595                 600                 605

Glu Thr Lys Gly Thr Gly Asn Asp Thr Val Leu Asn Val Ala Leu Leu
    610                 615                 620

Asn Val Ile Ser Asn Gln Glu Cys Asn Ile Lys His Arg Gly Arg Val
625                 630                 635                 640

Arg Glu Ser Glu Met Cys Thr Glu Gly Leu Leu Ala Pro Val Gly Ala
                645                 650                 655

Cys Glu Gly Asp Tyr Gly Gly Pro Leu Ala Cys Phe Thr His Asn Cys
            660                 665                 670

Trp Val Leu Glu Gly Ile Ile Ile Pro Asn Arg Val Cys Ala Arg Ser
        675                 680                 685

Arg Trp Pro Ala Val Phe Thr Arg Val Ser Val Phe Val Asp Trp Ile
    690                 695                 700

His Lys Val Met Arg Leu Gly
705                 710
```

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 bases
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: cDNA to mRNA
(A) DESCRIPTION: This is an oligonucleotide used with SEQ ID NO:10 to form a 5'end adaptor to construct the cDNA in SEQ ID NO:7

(i v) ANTI-SENSE: no

(x) PUBLICATION INFORMATION:
(K) RELEVANT RESIDUES IN SEQ ID NO: 1: FROM 1 TO 27

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:9:

GCGAATTCCA CCATGGGGTG GCTCCCA 27

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 bases
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: cDNA to mRNA
(D) DESCRIPTION: This is an oligonucleotide used with SEQ ID NO:9 to form a 5'end adaptor to construct the cDNA in SEQ ID NO:7

(i v) ANTI-SENSE: yes

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(x) PUBLICATION INFORMATION:
(K) RELEVANT RESIDUES IN SEQ ID NO: 1: FROM 1 TO 31

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:10:

AATTTGGGAG CCACCCCATG GTGGAATTCG C 31

I claim:

1. The recombinant protein coded for by the DNA sequence located at D3F15S2 locus on human chromosome 3 having 18 exons coding for a human growth factor, said human growth factor comprising an approximately 80,000 dalton, single-chain protein containing four Kringle Domains.

2. The recombinant protein claimed in claim **1** having the amino acid sequence coded for by the cDNA of SEQ ID NO:1.

3. The recombinant protein claimed in claim **1** having the amino acid sequence coded for by the cDNA of SEQ ID NO:2.

4. The protein depicted in FIG. **1** and having the amino acid sequence of SEQ ID NO:8.

5. The recombinant protein claimed in claim **1** having the amino acid sequence coded for by the cDNA of SEQ ID NO:7.

* * * * *